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RECENT PROGRESS IN THE STUDY OF ALLOYS.

THE systematic knowledge that we possess concerning the chemical relations of the compounds formed by non-metallic elements with each other, and with the metals, renders it surprising that we should know so little about the nature of alloys, that is, of bodies in which only metallic elements occur.

A great deal of attention has been given to this class of substances, and many isolated facts are known concerning the properties of individual alloys, but general laws have yet to be discovered. Much of our knowledge is, in fact, the accumulated tradition of technical workers, and it would not be a far-fetched illustration to compare the present state of the chemistry of alloys to that of chemical science in general before the time of Boyle.

It is easy to point out some of the special difficulties to which this state of affairs is due. When non-metals combine with each other or with metals, the products, as a rule, differ widely in properties from the original substances; hence the separation of the product in a pure state is a comparatively easy task. But this is not the case when two metals combine to form a compound: hitherto no alloy has been discovered which is more volatile than the metals composing it, and, though differences in fusibility exist, they are hardly sufficient to permit of the isolation of pure substances from mixtures.

Moreover, compounds of two metals retain a metallic appearance, and electrolysis, which has thrown so much light on the other parts of chemistry, here fails us completely; for an alloy, whether it be a compound or a mixture, appears to conduct without separation into its component metals.[1] The fact that all metals and their alloys are opaque, and that on account of the high temperature at which they melt vessels of clay or other opaque substance must in general be used to contain them, enormously increases the difficulty of experiment. We cannot note by eye the stage at which a liquid ceases to be homogeneous, or study the appearance of the bodies which crystallise out one after another from solution.

Hence the problem of the nature of alloys, although it is in part a chemical one, has hitherto been most successfully attacked by physical methods. We shall therefore begin by briefly reminding our readers of Matthiessen's work, and then go on to the results arrived at by the late Professor Alder Wright, Professor Roberts Austen, and by Heycock and Neville. The main outcome of this work can be summed up in the statement—that mixtures of liquid metals obey those general laws of solution which have been so brilliantly developed in the last ten years.

We shall then consider the more purely chemical attempts that have been made to isolate alloys of definite formula, work principally due to Deville and Debray, Schützenberger, Osmond and Werth, Guillemain, Levy, Joanniss, Charpy, and Le Chatelier.

Matthiessen's remarkable experiments on the electrical conductivity of solid alloys drawn into wire [2] must ultimately find a simple explanation; but partly, perhaps, because solid alloys are more complex than liquid ones, no satisfactory explanation has yet been given, and therefore these experiments will not be described in the present paper. The same must for the present be said of Weber's work on the changes in the electrical resistance of alloys during

[1] Obach, *Pogg. Annalen. Ergänzungs*, bd. vii., p. 280, 1876; and Elsässer, *ibid.*, N.F., bd. viii., p. 455, 1879.

[2] *B.A. Report* and *Phil. Trans.*

melting,[1] and of Le Chatelier's interesting experiments on the connection between the temperature and the resistance of certain alloys.[2]

Matthiessen's theory that certain metals when added, even in very small quantity, to another metal bring the latter into an allotropic state, has been often quoted, but cannot be regarded as having borne fruit up to the present time. On the other hand, his distinction between alloys—which are: (1) a homogeneous solution of one metal in another; (2) a homogeneous solution of a definite chemical compound of the two metals in the one which is present in excess; (3) a mechanical mixture of two different liquids, each containing both metals, but in different proportions—has been a most useful one.

As an example of class (3) he gives the case of a mixture of equal parts of water and ether. This, if well shaken, would for a short time appear fairly homogeneous, although it really consisted of drops of water containing some ether mingled, but not mixing, with drops of ether containing some water; such a mixture would on standing separate into two layers.

It is probable that many alloys are of this class, although the separation into two layers is a slow one which is very far from being complete when the alloy is solidified by rapid cooling. It seems improbable that any alloy of this class can be thoroughly satisfactory for mechanical purposes, or can be sufficiently homogeneous to make its properties worth studying. For such an alloy when solid would be a sort of conglomerate or concrete, and although such a texture might not be inconsistent with mechanical strength if a sufficient uniformity of grain could be ensured, yet it would be difficult to prevent parts of the mass differing in character. Moreover, differences in the coefficients of expansion of the two materials would be a cause of weakness. Professor Roberts Austen says that alloys of iron and aluminium containing from 40 to 60 per cent. of aluminium disintegrate spontaneously into clean metallic grains when

[1] *Annalen*, N.F., bd. 34, p. 576, 1888.

[2] *Zeitschrift für Physikalische Chemie*, bd. viii., p. 183, 1891.

kept for some months. This may be an extreme case of the weakness inherent in a conglomerate alloy.

A study of the proportions and temperatures at which the metals when melted in pairs form homogeneous liquids, ought therefore to be the first step in a scientific study of alloys. Matthiessen was aware of the importance of this subject, and made experiments on the miscibility of pairs of metals; but the later experiments of Alder Wright are more accurate and are the only ones we shall quote.

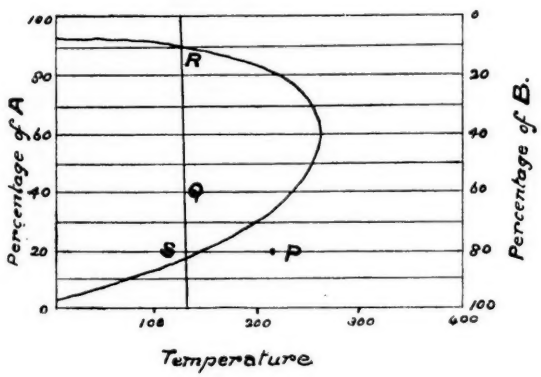
The behaviour of partially miscible liquids to one another has, however, been much more perfectly studied by Alexejew[1] and Konovalow.[2] These experimenters did not examine metallic solutions, but it is almost certain that the general conclusions they arrived at are applicable to alloys. The facts, so far as they affect our subject, can be very briefly stated. If a liquid B is gradually added to another liquid A and the mixture is sufficiently stirred, we shall at first get a homogeneous liquid, which may for convenience be called a solution of B in A. Continued addition of B will make this solution stronger, but it will remain homogeneous until A is saturated with B. A further addition of B, or the removal of some A by evaporation or freezing, will now cause the appearance of a second layer of liquid not miscible with the first. This new liquid may appropriately be called a saturated solution of A in B. A further addition of B will not alter the composition of these two layers, but will cause the second layer to increase at the expense of the first, and if we add enough of B the first layer will disappear and we shall have only the saturated solution of A in B, while with a still further addition of B we shall obtain an unsaturated solution of A in B. In other words, there is an infinite number of different proportions in which A and B may be shaken up together so as to give two layers of liquid, and in all cases the composition of these two layers will be independent of the proportion of A and B employed. These two layers of

[1] *Wied. Annalen*, 28, 305, 1886.
[2] *Ibid.*, 14, 219, 1881.

liquid, which can exist in presence of each other without change, may conveniently be termed *conjugate*.

The above applies to experiments conducted at a constant temperature. If we work at a higher temperature the compositions of the two conjugates will be altered. In general, raising the temperature will cause B and A to become more soluble in each other; so that the two conjugates approach each other in composition as the temperature rises, until finally a critical temperature is reached at which the two conjugates have the same composition, and, therefore, are indistinguishable from one another. At this and all higher temperatures the system will consist of one homogeneous liquid, that is to say, A and B will be miscible with each other in all proportions. Conversely, if A and B are mixed at a temperature above the critical, and the resulting homogeneous liquid be gradually cooled, a temperature will be reached at which the liquid will separate into conjugate layers. If temperature be plotted horizontally and the percentage composition of the mixture vertically, the composition of every possible pair of conjugates will be given by points on a curve, as in figure 1; and

FIG 1.



the two points lying on the same vertical will correspond to a pair of conjugates. Every point in the area of the figure corresponds to a definite state of percentage composition and temperature, but the points, such as P, R, or S, which

are on or outside the curve, are the only ones which correspond to a homogeneous solution. A point such as Q, which is inside the curve, corresponds to an imaginary solution, for such a state would break up into the two conjugates R and S which lie on the same vertical as Q. For example, a mixture of copper and tin, containing a large percentage of both metals, is probably a real solution so long as the temperature is sufficiently high ; but, long before solidification commences, it probably begins to separate into two conjugate alloys. This process may, through the action of gravity, result in any degree of heterogeneity, even to the formation of two layers of liquid if the cooling is slow enough.

These facts have been very little studied in metallurgy, except unsystematically by the technical worker, who has often found his bronze liquating or, apparently, separating into its constituent metals as it cools.

Alder Wright[1] has shown that at temperatures in the neighbourhood of 750° C. a mixture of lead and zinc separates into conjugate alloys containing respectively 1·3 per cent. of zinc in the heavier, and 1·57 per cent. of lead in the lighter alloy. He has shown that at 650° C. the zinc-bismuth conjugates contain respectively 14·28 per cent. of zinc, and 2·32 per cent. of bismuth, the increase in solubilities being just noticeable at 800° C. In the case of lead and aluminium at 800° C., the lead layer contained ·07 per cent. of aluminium, and the aluminium layer contained 1·91 per cent. of lead.

No attempt has been made to plot the curve of conjugates, similar to figure 1, for a pair of metals, and so to find the critical temperature of complete miscibility. The research would be a laborious one, but it might be carried out by using Alder Wright's methods, supplemented by a thermo-couple or a platinum resistance thermometer to measure the temperatures.

A research of more immediate importance for the art of metallurgy would be the determination of the composition

[1] *Proceedings R.S.*, 45, 48, 49, 50, 52, 55.

of the conjugate alloys of pairs of metals at the temperatures at which solidification commences; in other words, of the solubilities of the two metals in each other at the commencement of solidification. The writer is disposed to think that these solubilities at the freezing point, the eutectic[1] alloys in fact, give the limiting proportions in which the metals can be usefully alloyed for metallurgical purposes. A few of these solubilities have been published by Heycock and Neville, but as yet only one conjugate of each pair has been studied, and the metal pairs most useful in metallurgy, such as copper-tin, copper-zinc, and copper-aluminium, have not been discussed. A careful study of the cooling curves obtained by Roberts Austen would perhaps give us these solubilities.

Conjugate solutions, such as those above described, have been found by Konovalow[2] to possess a remarkable property. It is this, that if either or both of the components be volatile, then the vapour given off by each of the two conjugates is identical in pressure and in composition, though the two conjugate liquids may be very different from each other. Consequently the two conjugates would begin to boil at the same temperature. This property is not at present of importance in the case of conjugate alloys on account of the low vapour pressure of the metals at the temperatures we can command; but, as Ostwald has pointed out, a corresponding property as to the temperature at which a pair of conjugates would refuse to dissolve either of the metals in the solid form may be important. It seems probable from theoretical considerations, that if the pair of conjugate alloys be formed at so low a temperature, that one of them is saturated with the solid metal A; then the other conjugate is also saturated with A at the same temperature. If heat is now subtracted from either conjugate the first result will be the same, namely, the precipitation of solid A. Continued abstraction of heat will, however, affect the two alloys differently—that richest in A will be

[1] That mixture of two substances which has a lower melting point than mixtures of the same substances in other proportions is said to be *eutectic*.

[2] *Loc. cit.*

gradually converted at a constant temperature into its conjugate, with precipitation of A, while the other conjugate, if heat be taken from it, will slowly cool with precipitation of A.

ON TERNARY ALLOYS.

Practical metallurgists have long ago recognised that the addition of a third metal to an alloy materially alters its properties, and the number of ternary alloys, or mixtures of three metals, that have been devised for special uses is very large, many different alloys being used for the same purpose by different manufacturers. A good deal of light has been thrown on this complicated subject by the researches of Alder Wright.[1] Developing facts previously studied by Duclaux[2] in the case of mixtures of water, ether, and alcohol, he has shown that if we take two partially miscible liquids, such as lead and zinc, in such proportions that the mixture separates into two conjugate alloys, then by the addition of a third metal, such as tin, which is freely soluble in both the others, we can increase the solubility of the lead and zinc in each other. The two conjugates can thus be made to approach each other in composition, and a sufficient amount of tin will make them identical, so that for this and all higher proportions of tin, the three metals will form a homogeneous mixture. The third metal thus acts somewhat like a rise in temperature in Alexejew's experiments (fig. 1).

It is not improbable that the beneficial effect of the third metal in many alloys in use, is due to its thus rendering the mixture of the other two homogeneous. Alder Wright's method of experiment was to melt the three metals together in the desired proportion and pour the mixture into a long narrow crucible of clay, which was maintained for several hours at a constant temperature well above the melting point. The alloy was then rapidly cooled, and the upper and lower parts of the ingot analysed. In those cases where the amount of the third metal was insufficient to

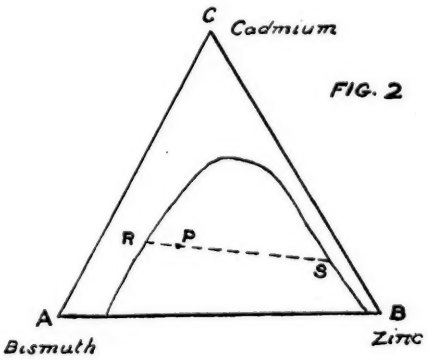
[1] *Loc. cit.*

[2] *Annales de Ch. et Ph.* (5), 7, 264, 1876.

prevent separation, the ingot was seen to consist of two layers having a well-marked dividing surface between them.

His results admit of being very elegantly expressed by a method suggested by Sir George Stokes. Suppose that a mixture be made containing *a* per cent. of A, *b* per cent. of B, and *c* per cent. of C; then, if we draw an equilateral triangle A B C and find the centre of gravity P of masses *a*, *b*, *c*, placed at the corners A B C respectively, the point P will record the composition of the mixture. Conversely, every point in the area of the triangle represents a different mixture. For example, the point P in figure 2 represents a mixture of two parts of A, one of B, and one of C.

Now, Alder Wright's results show that if the percentage



of the third metal C, which mixes freely with both A and B, and may therefore appropriately be called the solvent, be small enough, that is, if P be near enough to the line A B, and not too near either A or B, then the alloy represented by P separates into two conjugates represented by the points R and S lying on a straight line through P. If a series of mixtures of A, B, and C in different proportions be examined, and the conjugates into which they divide be found by analysis of the upper and lower parts of the ingots, we can plot a series of points, such as R S. The curve passing through all these is called the *critical curve*. Figure 2 gives Alder Wright's critical curve for mixtures of bismuth, zinc, and cadmium at 600° C.

Alder Wright has traced the critical curve for the following cases, the first named metal of each triad being the solvent metal.

Sn, Pb, Zn	
Sn, Bi, Zn	
Sn, Pb, Al	
Cd, Bi, Zn	
Cd, Pb, Zn	
Sb, Pb, Al	
Sb, Bi, Al	
Ag, Bi, Al	
Ag, Bi, Zn	

A critical curve having been determined we can at once predict from it whether a proposed mixture will remain homogeneous or will separate into two layers. If the point corresponding to the mixture be plotted, and lies on or outside the critical curve, the alloy will be homogeneous; if it lies inside, the alloy will split into conjugates. A critical curve must of course be constructed as the result of a series of experiments, carried out at a constant temperature. If the temperature rises, the curve shifts, generally in the sense that the higher the temperature, the smaller is the area inside the curve; that is, the less solvent is needed to make a homogeneous or *real* alloy. The Bi Zn Cd curve given in figure 2 is very sensitive to change of temperature.

If the critical curves of the triads of metals, habitually used together in the arts, were determined at the lowest temperatures compatible with perfect fluidity, we might perhaps find in them a rational basis for predicting the proportions of the metals to be employed in the most useful alloys.

Alloys which were *real*, in the above sense, would probably prove to be mechanically homogeneous when solid; although even in these, a microscopical examination would in most cases show structure.

THE SOLIDIFICATION OF ALLOYS.

In studying the process by which an alloy solidifies observations with the thermometer are of great value. For, so long as the mass of cooling substance remains completely liquid, and abrupt chemical changes do not take place, a thermometer immersed in it will indicate a uniform rate of cooling, but the separation of solid matter will be marked by the evolution of heat, of fusion or solution. If the formation of solid matter is gradual and con-

tinuous, as will be the case when some of the solid is already present, the thermometer will indicate a slower rate of cooling, or, if the system is protected from too rapid loss of heat, the temperature may become constant for a time. But molten metals, like other liquids, show the phenomenon of *surfusion*, that is to say, the liquid, if no solid is present, can be cooled below its proper melting point. It is then in an unstable condition, and sooner or later this state ends by the rapid formation of a considerable amount of solid with the evolution of a corresponding amount of heat. If the system is so arranged that losses of heat by radiation and conduction are slow, the heat evolved at this stage may raise the temperature of the whole mass considerably, the highest temperature attained being at, or very nearly, that at which solid and liquid can exist in permanent equilibrium. This temperature, the freezing point as it is convenient to term it, is thus often indicated by the thermometer with great delicacy.

If we are dealing with a pure metal the freezing point is remarkably constant, the temperature after the period of surfusion is over, remaining absolutely the same until the whole mass is solid. Conversely, if heat be slowly added to a mass of the pure solid metal, the temperature will become constant as soon as fusion commences, the melting and freezing points being absolutely identical.

When the metal is no longer pure, but is alloyed with a small quantity of some other metal soluble in it, the process of solidification obeys the law of Raoult. The metal present in excess, which we may term the solvent,[1] no longer solidifies at its true freezing point; but it does not begin to do so until a lower temperature is reached, the pure solvent separating at continually lower and lower temperatures as the liquid becomes a stronger solution of the dissolved metal.

[1] When two substances are mixed and form a homogeneous liquid, it is difficult to give a rule for deciding which of the two is the solvent. There is a tendency to regard that substance as the solvent which separates out in cooling. But this rule breaks down when we consider the cooling of a saturated solution.

In the case of dilute solutions the depression of the freezing point below that of the pure solvent is found to be directly proportional to the percentage weight of dissolved metal and inversely proportional to its atomic weight. But if we continue to increase the strength of the solution a concentration will be reached at which the solvent is saturated with the dissolved metal. A further addition of this metal will then have no effect on the freezing point of the solution; we shall have reached the eutectic state. The freezing point of such a mixture is as steady as that of a pure substance; the whole mass solidifies at a perfectly constant temperature, and if there is no excess of either metal the resulting solid will be remarkably homogeneous. Many cases of this kind have been studied.

If we plot horizontally the percentage of the dissolved metal B, and the depression of the freezing point be plotted vertically downwards, we can by adding weighed quantities of B to the mixture, and determining the freezing point after each addition, get a series of freezing points which will lie on the broken line L M N (fig. 3). The

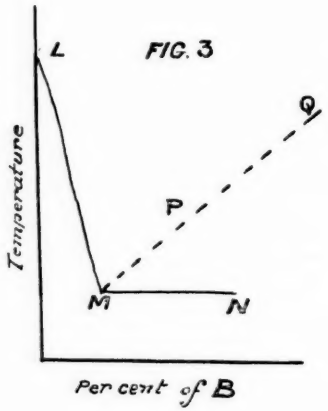


FIG. 3

point L is the freezing point of the pure solvent A, and the horizontal line M N gives the constant freezing point of the eutectic alloy, a temperature which is independent of the excess of B that may be present. If B is sparingly soluble in A the line L M will be very nearly

straight, and its exact solubility at the eutectic temperature can be determined by producing the lines L M and N M to cut each other.

If the solubility of B in A decreases fairly rapidly as the temperature falls, another series of freezing points exists lying on the dotted line M P Q. These indicate the temperature at which the cooling alloy becomes saturated with B, and consequently either B begins to separate or the liquid splits into conjugates. Heycock and the writer[1] have lately succeeded in tracing this line of freezing points; but except when B is present in large excess there is very little solid matter formed at them, and the indication of the thermometer is of a most fugitive character. This phenomenon is not to be confounded with a real rise in the freezing point of the whole alloy, such as that caused by adding silver to cadmium.

The osmotic theory of solution, due to Van't Hoff, leads to the conclusion that $\delta = \frac{1{\cdot}98T^2}{M\lambda}$, where δ is the depression in the freezing point of M grams of the solvent due to the solution in it of one gram-molecular weight of any substance, λ being the latent heat of fusion of the solvent and T its freezing point reckoned from the thermodynamic zero (-273° C.).

If we take as solvent 100 atomic weights of one of the metals in the table below, then δ, the depression predicted by the theory as due to one molecular weight of dissolved body, is given by the numbers in the table in degrees centigrade.

Tin	Bismuth	Cadmium	Lead	Zinc
3° C.	2°	4·5°	6·5°	5·2°

It has been found by Heycock and Neville[2] and by Tammann[3] that in a large number of cases these depressions are produced by the addition of one *atomic weight* of

[1] We hope shortly to publish the experiments bearing on this point.

[2] *Chem. Soc. Jour.*, lvii., 376, 1890; and lix., 888, 1892.

[3] *Zeitschrift Phys. Ch.*, bd. iii., 441, 1889.

dissolved metal. It follows, if the theory can be trusted, that the molecule of a metal when in dilute solution consists of *one atom.* There are numerous exceptions to this rule; for example, aluminium when dissolved in tin appears to form diatomic molecules, and the same is true for zinc palladium and mercury when one of these metals is dissolved in cadmium.

But the nature of the solvent has certainly an influence, over and above that attributed to it by the above formula, in determining the depression; and from what follows it will be seen that the aggregation of the dissolved body into more complex molecules is not the only possible explanation of these abnormally small depressions.

In a few cases the dissolved metal, instead of causing a depression in the freezing point of the solvent, produces a rise. Antimony dissolved in either tin or bismuth, and silver in cadmium or in zinc, produce this effect.

In these cases of a rise in the freezing point experiment has shown that the portion of the mass which solidifies first, instead of being the pure solvent, is richer in the dissolved metal than either the original liquid or the still fluid portion. Van't Hoff[1] has given a theory which fully accounts for this phenomenon. He shows that whenever the matter which separates first contains both metals in the form of a homogeneous mixture, or, as he terms it, a "solid solution," there will either be a diminished depression or a rise in the freezing point. It is worthy of note that in these cases we observe, not the formation of a small amount of solid, but a real rise in the temperature at which the mass of the alloy solidifies and sets in the solid form, even when less than 1 per cent. of the second metal has been added.

If we exclude for the moment cases in which the two metals are combining chemically, and these cases do not seem to be extremely common, it follows from what has been said, that a mixture of two metals in a completely molten state is either homogeneous or is a mechanical mixture of two conjugate liquids, each of which may be

[1] *Zeitschrift für Physikalische Chemie*, bd. v., p. 332.

called a saturated solution of one metal in the other. The proportions in which the two metals were mixed will determine the relative quantities of the two resulting liquids, but will not affect their percentage composition. When the temperature falls the two conjugates will alter in composition, and when solids begin to separate we may expect to find considerable complexity in the resulting body without the necessity of assuming chemical combination to have taken place. Let us consider the case of the metal A, having a high melting point and present in such excess that the second metal B, with a lower melting point, is completely soluble in it. Moreover, let the mixture be above the temperature L at which A melts. If we now slowly cool this homogeneous system one of two things will happen, it may separate into conjugates or it may remain homogeneous until pure A begins to separate out in the solid form at a temperature M below the freezing point L of the pure substance A.

We will consider the latter case. If a thermometer be immersed in the mixture, it will indicate a short period of stationary temperature as soon as A begins to crystallise out; this is the first freezing point. As A continues to separate the solution of B in A becomes stronger, and, in virtue of the Raoult law, A will crystallise out at a continually lower and lower temperature. But a moment must come when, on account of the removal of A in the solid form, the remaining liquid becomes saturated with B. The conjugate of this liquid will now begin to form, and as A continues to freeze out, more and more of this new liquid will be produced at the expense of the first; but during this stage neither liquid will alter in composition, and therefore we should expect A to continue separating at a constant temperature N. As soon as the new saturated solution of A in B is the only liquid left, the temperature will begin to fall with continued separation of A or perhaps of solid conjugates of the remaining liquid. This fall in temperature will continue until the liquid is saturated both with A and B, that is until we have reached the eutectic solution of A in B at the temperature P. From this point A and

B will separate together as solids, or very probably as a solid solution, and the body will remain at a very constant temperature until it is completely solidified. Figure 4 gives

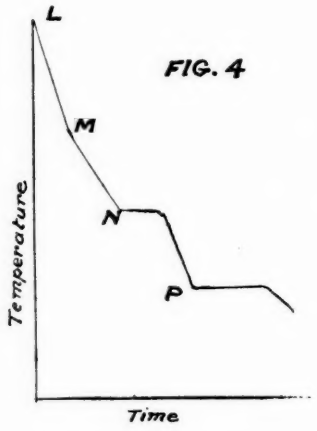


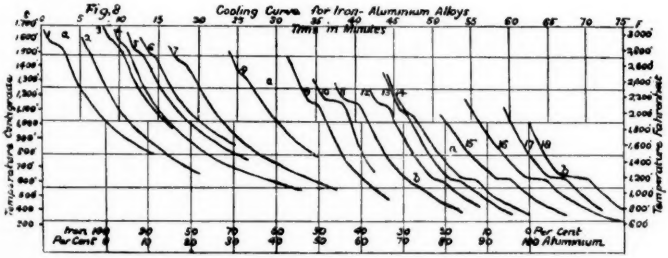
FIG. 4

a diagrammatic representation of these stages in the cooling, temperatures being measured vertically and times horizontally from left to right. Whenever there is a decrease in the rate of cooling due to the separation of solid matter, we shall see in the cooling curve an angle as at M, or if an isothermal transformation is taking place as at N and P there will be a flat.

It is obvious that in an alloy containing but little B, the point M will be well marked because a large amount of A can solidify before the concentration, and therefore the freezing point alters perceptibly; in fact in very dilute solutions there may be a flat at M. With a stronger solution of B the point M is harder to detect and may be missed altogether. The length of the two flats at N and P will depend on the proportions and on the solubilities of the two metals. The temperature M will depend on the amount of B present. The temperature at P, in the eutectic state, is quite independent of the original proportions of the two metals, and, in the case of one or two pairs of metals known to the writer, this is true for the transformation which begins at N. But it must be confessed that, in most

of the binary alloys that have been examined, the temperature from N onwards does depend somewhat on the original proportions of the two metals, and that this stage does not appear to be altogether isothermal. An impurity would produce this effect, but it may be that some other cause is at work.

It would probably require a very delicate thermoscope to detect all these details during the cooling of one alloy, but the whole series is well shown in the cooling curves of iron-aluminium alloys (fig. 5). This figure is taken from



Professor Roberts Austen's "Third Report on Alloys".[1] The curves were obtained by an automatic method of observation. A thermo-junction was placed in the centre of the mass of molten alloy, and a galvanometer in the circuit projected a spot of light on to a sensitive plate. The plate possessed a uniform motion of translation at right angles to that of the spot of light from the mirror of the galvanometer. In this way, as the cooling progressed and the electromotive force of the thermo-couple, and consequently the current passing through the galvanometer, decreased, curves were traced out in which the rate of cooling is indicated by the slope of the curve. Each curve in the figure belongs to an alloy of different composition, the point where each curve cuts the line of 1000° giving the percentage composition, which can be read off from the scale at the base of the figure.

It will be seen that all the curves approach the horizontal at low temperatures. This is due to the fact that

[1] *Engineering*, 1895.

the rate of cooling of any substance is necessarily greater, the greater the difference in temperature between it and surrounding bodies, and this feature in the curves has no special meaning.

On examining these curves we see that the upper part of numbers 1 to 7 contains a well-marked flat due to the Raoult effect, and that this becomes fainter as the percentage of aluminium increases. From 9 to 12 we see a series of flats occurring at a nearly constant temperature, corresponding probably to the formation of conjugate liquids, while from 12 onwards in the alloys rich in aluminium we see a well-marked flat rather below the melting point of aluminium (654°). This occurs at exactly the same temperature in each case, and is certainly the eutectic flat for aluminium saturated with iron. The copper-tin and copper-bismuth curves given by Roberts Austen show similar features.

If the preceding analysis of the process of solidification be correct, then during the whole of the period from M to P (fig. 4) crystals of A or of a solid solution of B in A will be separating out and forming nuclei of solid matter, while from P onwards a liquid of constant composition will be solidifying in the spaces between the crystals already formed. This liquid which solidifies last is independent of the original percentage composition of the alloy, so that there is some danger of mistaking it for a definite compound. A structure corresponding to the above has been observed in the microscopical examination of alloys.

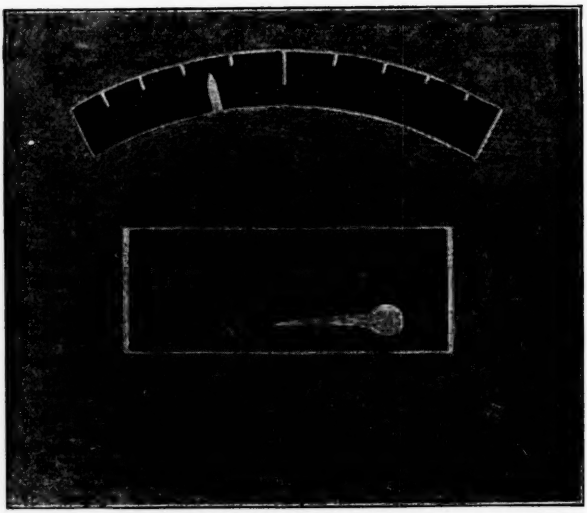
The cooling curve may be much modified in special cases. For example, it is conceivable that the freezing point of the eutectic solution of A in B might be above N instead of below it. In this case the flat at N will be prolonged, and the second flat will disappear. The same change in the diagram, though from different causes, will occur if the two metals are miscible in all proportions, like lead and tin or zinc and cadmium. Surfusion may sometimes cause a rise at the point M, and the formation of chemical compounds might profoundly alter the curve.

It appears probable that mechanical strength will largely

depend on the expansions or contractions that take place during the final solidification of the lower eutectic alloy. Behrens has found by microscopical examination that this most fusible alloy can sometimes be seen to have contracted in freezing, so that minute spaces are left between the less fusible crystals that form the bulk of the substance. Here we have a source of great weakness in a material that, to other than a microscopical examination, would appear homogeneous. Lead-gold and bismuth-gold alloys are probably examples of the same phenomenon. A very little lead makes gold brittle, because of the great contraction of the lead during the final stage of freezing. Perhaps the brittleness of a gold-bismuth alloy may be due to the considerable expansion which is known to take place during this final stage, a state of strain being thereby produced in the substance.

F. H. NEVILLE.

(*To be continued.*)



GALVANOTROPISM OF TADPOLES.[1]

GENTLEMEN, you have before you on the screen an image of a tadpole in a rectangular trough of water through which a galvanic current will be passed *via* two flat metallic surfaces forming the two short ends of the trough. Just above is the image of a galvanometric pointer, the movements of which will indicate the direction and strength of current. A commutator in circuit varies the direction of current, and a resistance that can be altered by turning a screw (*i.e.*, an Engelmann's screw-rheostat) serves to vary its strength. The curved scale projected with the pointer upon the screen is graduated in milliampères.

It is not enough to say that so many milliampères of current are used, we must also—in order to have some idea of what passes through the tadpole—know what is the "current-density" in the water. Obviously a current of say one milliampère will be of less density if it is passing through a wide than through a narrow column of water

[1] A Lecture in Electro-Physiology delivered by Dr. Augustus Waller, M.D., F.R.S., at his private laboratory, in June, 1895.—EDITOR.

with the same current-strength, through columns of 10 cm.^{2} and 100 cm.^{2} sectional area; the current-density in the first case is ten times what it is in the second. And the tadpole accordingly is traversed by more current in the first than in the second case.

To know where we are we must therefore agree upon some unit of current-density, and ascertain from measurement of the sectional area of the water column how many such units are passed through it, and—assuming the resistance of the tadpole to be equal to that of the water[1]—through the tadpole.

We shall take as the most convenient unit of this order the density afforded by 1 ampère through a column of 1 square metre sectional area, a value that we may denote by the symbol 1*a*.

You will best realise the notion of this unit by tabulating a few values:—

1 ampère	through	1 square metre	has the density 1*a*
1		0·5	2*a*
1		0·01	100*a*
1		1 square centimetre,	10,000*a*
1 milliampère,		1	10*a*
1		10	1*a*
1		5	2*a*
2		5	4*a*
etc.,		etc.	

The circumference of my wrist is 17 cm., *i.e.*, the transverse section is about 23 cm.^{2} If I stand say a current of 5 milliampères this implies an average current-density of $\frac{5}{23}$ milliampères per cm.^{2} $\frac{5 \times 10{,}000}{23}$ milliampères, *i.e.*, 2000 milliampères per square metre, *viz.*, 2*a*.

[1] The resistances are not equal, but this will not affect the dosage, which will be correctly enough expressed by the number of density units through the water. If the tadpole is in a fluid of lower resistance than itself it will receive less than its share of current, if in a fluid of higher resistance more than its share of current. This is easily verified by testing a tadpole in normal saline; when a far larger current is required to bring off the effects described.

The sectional area of the water in this trough has been made as nearly as possible 5 cm.², and since each division of the scale is 1 milliampère it follows that each half division indicates a current-density through the water (and through the tadpole) of 1*a*.

We may now proceed with an experiment. The tadpole is at rest; closing the circuit I pass through it a current of 1 milliampère (*i.e.*, of 2*a*). the animal is agitated and turns its head to anode, since its head is to the anode and its agitation takes the form of swimming movements, it swims to the anode and there stays quiet. I now reverse the current, the animal is agitated, turns round and swims across the trough to the new anode. I reverse again and the tadpole passes over again, always moving oppositely to the pointer, *i.e.*, against the current from kathode to anode.

This, however, has not been a perfectly typical experiment in so far as it has not clearly exhibited what—in agreement with Hermann who first made the observations, and in disagreement with Ewald who contradicted them—I have been led to admit as the fundamental fact.

It is not always possible to predict the direction in which a given tadpole will swim, nor that which it will finally occupy; it may and often does swim the other way, *i.e.*, towards the kathode, and there remain more or less quiescent as long as the current is passing. But if following Hermann's plan we observe a number of tadpoles in a large trough (Hermann's trough was 180 × 63 mm.) traversed by a moderately weak current (1 to 2*a*), we shall be able to see that a large number of tadpoles point motionless towards the anode, that others swim towards the anode, and that a few point and swim towards the kathode.

Here is what I find to be a "safe" and convenient form of experiment: two tadpoles are placed in a smaller trough (90 × 30 mm.) in the lantern-field, with a current of about 4*a*, alternated in direction two or three times; their, for this purpose, somewhat too exuberant vivacity is toned down, so that they no longer dart about upon the smallest provocation. They are somewhat sluggish, their move-

ments are, so to speak, more dead beat, and, in the absence of current, or even while the current is passing, the position of the long axis remains stable in any position, preferably antidrome, *i.e.*, with head to anode, but frequently homodrome, with head to kathode. In the antidrome position, as you may see, they are perfectly still as if paralysed, in the homodrome position they wag their tails. I wake them up by reversing the current; after a dart here and there they settle again and it may be in any position. Both may look up stream or down stream, or one may look one way, the other the other. And now, to quickly realise the relation between direction of current and position of tadpole, I am sure from my own hesitation, in spite of the pointer showing how the current is going, that you do not instantly recognise the sudden changes under the correct rubric, "homodrome," "antidrome". So let me use domestic language, and, comparing our tadpoles with cats, speak of the current as stroking them the right way, *viz.*, from head to tail, or stroking them the wrong way, from tail to head.

You will, I think, readily admit a valid excuse for such untechnical language when you have recognised by a rapid series of trials that stroking the right way pacifies, stroking the wrong way excites, *i.e.*, in technical language, arrest by an antidrome current, excitation by a homodrome current. The tadpoles happen to be lying side by side and I cautiously stroke them the wrong way by gradually putting on current with the screw-rheostat, they both wag their tails. I cautiously reverse the current, unscrewing the rheostat, reversing, then screwing again, guiding myself as to current-strength by the current indicator; the tadpoles, which are now being stroked the right way, lie perfectly still. Or better still, having been stirred up to greater activity by sudden reversal or reversals of current, they have come to rest side by side with their heads in opposite ways; and now I am able to play at see-saw, by cautiously putting on current and cautiously reversing it. Always the tadpole stroked down the wrong way wags his tail, while his companion, who is at the same time being stroked down

the right way, remains perfectly still; and on reversal of the current the behaviour of the two individuals is reversed, *e da capo.*

So that, with Hermann, we may be satisfied to conclude that the essential fact upon which the galvanotropic effect turns is that current down the animal has a quieting action, current up the animal an exciting action.

The presence of the spinal cord is an indispensable condition of the success of the experiment. In this trough I have now placed two tadpole tails, one cut off near the head, the other about half-way down; the first includes a bit of spinal cord, the second does not; both tails lie along the line of current, which, as you see, causes the first tail to tremble when it passes in an upward direction. There is not a tremor to be seen when the current passes in an opposite direction, *i.e.*, towards the tip. The other tail, *viz.*, that without spinal cord, remains motionless with both directions of current.

We are now properly prepared to see more clearly than would otherwise have been the case the *rationale* of the experiment in its first and most striking form, as first witnessed and described by Hermann.

This flat trough (100 × 75 mm.), about as large as will fit the lantern, contains a number of fresh tadpoles, moving more or less leisurely and jostling each other in all directions. I suddenly close a key, sending through the water and the tadpoles a current of about 3*a*. The commotion is amazing, the tadpole community seems to have gone mad, a writhing mass is all that can be distinguished; but the disturbance does not take long to subside, and now all the tadpoles are fixed as if at attention looking one way, heads to anode, *viz.*, traversed by a current from head to tail, stroked down the right way. This is galvanotropism in so far as it is an orientation of the body under the influence of the galvanic current, but it is hardly galvanotropism of a simple and fundamental character analogous with the galvanotropism of protozoa, or the heliotropism of plants. It is a reflex adjustment of the animal to its environment effected through the agency of the nervous system; the tadpoles have ex-

perienced excitation in all positions of the body but one; the position of least excitation, or we must even say the most soothing position, is enforced upon them by that experience. Stroking the wrong way excites them, they therefore avoid the positions in which that happens. Stroking the right way pacifies them, and they therefore adopt the positions in which that is best received.

GALVANOTROPISM.

In the lowest forms of animal life—amœbæ, infusoria, etc.—the polar response to excitation by the constant current is diametrically opposed to that obtaining upon differentiated muscle and nerve. Whereas upon the latter the make excitation is kathodic, and the break excitation anodic, upon non-fibrillated protoplasm the make excitation is anodic and the break excitation kathodic. With these effects there is in many cases a remarkable orientation in relation to the current—"galvanotropism"—accompanied in some instances by an evident disintegration of protoplasm on the anodic side (*e.g.*, in Actinosphœrium and in Pelomyxa), in others (*e.g.*, in Paramœcium), by amœboid or swimming movements in the direction of the current, *i.e.*, away from the anode. In general the orientation of Infusoria is such that they arrange themselves longitudinally in the lines of current with their anterior ends towards the kathode, and their swimming movements, if any, in that direction (*e.g.*, Paramœcium); in some instances (*e.g.*, Polytoma uvella, Cryptomonas erosa), the orientation is reversed; in others again it is transverse, the long axis of the animal disposing itself at right angles to the current (Verworn).

Fertilised frog's eggs exhibit according to Roux very remarkable galvanotropic effects; in a layer of spawn traversed by strong alternating currents (100 volts), each individual egg presents at the end of a few minutes a division into three zones—two dark polar areæ separated by a light equatorial zone—and the eggs collectively dispose themselves in conformity with the lines of current-diffusion so that the light equatorial stripes lie at right angles to the lines

of current, thus indicating the general direction of equipotential curves (which we know to be at right angles to the lines of current).

A curious sight is offered by the behaviour of a drop of hay-infusion, containing paramœcia in sufficient abundance, placed in a flat vessel into which dip the unpolarisable electrodes of a battery of 2 to 5 volts. At make the whole crowd of paramœcia fall into order with their noses towards the kathode, and begin to swim towards it in converging curves; in a few minutes they are thickly crowded round the kathode, and the fluid round the anode is quite cleared; if now the direction of the current is reversed, the crowd breaks up, all its units turn round and begin to swim away as if of one mind from the new anode to the new kathode, to which the crowd converges as before.

There does not seem to be any unanimity among the protozoa as to the direction they shall adopt in relation to the current. Paramœcia swim with the current from anode to kathode; in this little electric bath you can follow them with the naked eye, but I will throw them upon the screen, when you will see them better still. As I put on the current they turn with one accord to the kathode and swim to the kathodic bank of their lake, as I reverse the current they turn round and swim over to the other bank; there happen to be not very many paramœcia in this infusion. What is happening on the screen is absurdly like what one may see in the country; these little brown spots swimming across their lake from bank to bank look just like rabbits scampering across a field from one cover to another, and as we reverse the current they scurry across backwards and forwards as if beaten out of cover as soon as they have found it. If one reverses the current at a moment when they are scurrying across at the top of their speed, they turn themselves and rush off the other way.

Ciliated infusoria, as a rule, agree with paramœcia and swim with the current. The custom among flagellata, on the other hand, is to swim the other way; they affect the anode or the anode affects them. It is difficult to resist laughing when one has under one's eyes the spectacle of a

galvanic bath such as this, containing a mixture of ciliated and flagellated protozoa. In the absence of any electrical current they are swimming about in all directions, intermingling in the most friendly manner. Make the current and two armies, so to speak, assemble themselves on the two banks; ciliata to the kathode, flagellata to the anode! appears to have been their *mot d' ordre;* and now if you reverse the current the two armies put themselves in motion and appear as if precipitating themselves upon each other, but no disaster happens, the opposing crowds slip through each other and reassemble at the pole which they respectively affect.

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AUGUSTUS WALLER.

THE CHROMATOPHORES OF ANIMALS.

THE wide distribution of pigments throughout the tissues of animals, the differences in origin, nature, and function which they present, and the variety of forms under which they are manifested, render the exact definition of the term chromatophore in the present condition of knowledge a matter of some difficulty. The term has indeed been restricted by Pouchet to the pigment bodies of Cephalopods, and a distinction has been drawn by him between these structures and the pigment-cells of Vertebrates, which he has termed chromatoblasts. As it is now, however, indisputable that the pigment bodies of Cephalopods are true cells, it is no longer possible to restrict the term in this way: chromatophore and chromatoblast are synonymous.

Chromatophores may safely be defined as pigmented cells; but all pigmented cells are not chromatophores. We have to distinguish the essentially chromatic cell from other pigmented cells whose colour, as such, is immaterial. The question is one of limitation: which pigmented cells are chromatophores? It would be meaningless, for example, to apply the term chromatophore to pigmented cells of the excretory, or respiratory, or sensory tissues. By following this principle of elimination the physiological answer to the question becomes apparent: chromatophores are pigmented cells whose essential function is chromatic, that is, to bestow particular colours upon an animal. In the case of respiratory or nutritive pigmented cells the colour is unessential, and is a mere attribute of the particular respiratory or nutritive bodies, as blue is an attribute of copper sulphate; but in the case of chromatophores the colour is all in all, and the nature of the pigmented bodies altogether immaterial.

The difficulty is to draw the line. In the cuttle-fish or frog the chromatophores are easily recognisable owing to their highly specialised form and their readily demonstrable function. But what are we to do in those numerous cases

of highly coloured animals in which the value of colour is still hypothetical, and in which there is no peculiarity of form to distinguish any purely chromatic cells from other pigmented cells which may be inferred to discharge respiratory, nutritive or other functions? The Turbellaria and Echinoidea afford cases in point.

Two attitudes are possible. The term chromatophore may be applied to all pigmented cells which have not been shown to discharge a respiratory or other non-chromatic function; or it may be restricted to pigmented cells which are without doubt chromatic in function. The latter attitude seems to me preferable, since it begs no question and yet conduces to precision of language.

Chromatophores are thus pigmented cells specialised for the discharge of the chromatic function.

This definition evades the difficulty presented by pigmented cells which, although respiratory or excretory, etc., in function, do, nevertheless, contribute to the normal coloration of the animal, as, for example, the elements of the vasofibrous tissue of leeches. There still remains the question whether the term chromatophore is applicable to the cells of an epithelium in which pigment is deposited for indubitably chromatic purposes, but which are not distinguished by any other features from the unpigmented elements of the same tissue. This case is presented by the Insecta and Brachyura, in which groups the colours of the pigments deposited in ordinary cells of the epidermis (hypodermis of authors) frequently assume a high protective significance. It is far from improbable that the distinctly specialised chromatophores of other Arthropods have been developed from such unspecialised pigmented cells as those of the Insectan epidermis, so that the latter may certainly be regarded as incipient chromatophores; but the fact that they are in no way set apart for chromatic purposes, that this function is merely superadded to their ordinary task of secreting the protective cuticle of the body, seems to me to be decisive against their claim to the title chromatophore in any other than a purely etymological sense.

With the ground thus cleared we may proceed to the

more immediate object of the present paper, namely, to reveal what light has been thrown by increase of research upon the evolution and mechanism of true chromatophores.

Since it is evident that chromatophores are simply pigmented cells specialised for a particular purpose, the problem of their evolution cannot be adequately considered except by the comparative method, which in this case involves a survey of pigment-cells in general.

In this survey special attention has been paid to two points :—

i. The localisation of the pigment-cells and their relation to the germinal layers.

ii. The nature of the structural modifications exhibited by pigment-cells.

I have neglected all references to intercellular pigmentation, since this phenomenon, important as it is in regard to the history of pigment-cells in general, has no particular bearings upon the origin of chromatophores.

1. *Porifera.* Pigment-cells of oval, spindle-shaped, or stellate forms are described by Schulze and Vosmaer for various non-calcareous sponges. Their origin appears to be unknown (Vosmaer, *Bronn's Klassen und Ordnungen*, ii., 1887).

2. *Cœlentera.* In the Hydrozoa pigment may be deposited either in the ectoderm or in the endoderm. The varied colours of the Hydroidea, especially the Gymnoblastea, are almost entirely due to pigmentation of the endodermal cells (Allman), but ectodermal pigment is found in the ocelli of Craspedote Medusæ and occasionally in the epithelium covering the generative glands (Hertwig).

The brilliant colours of many Acraspedote Medusæ appear to be chiefly due to pigments deposited in the ectoderm (Haeckel).

In the Anthozoa the brilliant colours are chiefly due to so-called zooxanthellæ, which have been interpreted by the Hertwigs as symbiotic algæ. The earlier observers (Haime, M. Edwards, Gosse) described a special pigmented layer of the ectoderm; but Heider has failed to find any special pigment-cells, and he attributes the

markings of the oral disc in *Sagartia troglodytes* to the distribution of the various coloured ectodermal gland-cells (*Sitzungsberichte Akad. Wiss. Wien*, lxxv., p. 394, 1877). The brown colour of the column and base of *Sagartia parasitica* is caused, according to the Hertwigs, by the pigmentation of "connective tissue cells" within the mesoglœa (*Die Actinien*, p. 45, 1879).

The highest development of the pigment-cell in Cœlentera is found in the Ctenophora, and in this group the pigment-cells are exclusively ectodermal. Apart from the "glance-cells" and fluorescent cells of *Cestus Veneris*, the former of which seem to foreshadow the iridocytes of higher forms, rose-coloured pigment-cells are found in *Callianira*, and beautiful chromatophores, yellow, brownish-red, or rose in colour, deck the external epithelium of various species of *Beröe* and of *Euchlora rubra*. The chromatophores of *Beröe* are stellate, and contract upon stimulation; they are developed from simple unbranched cells of the ectoderm (Chun).

3. *Turbellaria*. In Rhabdocoelida the body colours are seated as a rule in the sub-epidermic parenchyme (L. von Graff). The pigments may be either (1) granular (the usual type) and distributed in connective tissue cells, *e.g.*, most Acœla, or in fibres of the parenchyme, forming a reticulum; or (2) in solution, either (*a*) diffused throughout the protoplasm of the cell, or (*b*) restricted to one or several intracellular vacuoles, *e.g.*, various species of *Vortex*.

When the pigment is ectodermal it may be either (1) granular, (2) in solution and diffused through the cell-body, or (3) in the form of coloured rods, *e.g.*, *Convoluta flavibacillum*.

Among Dendrocoelida the colour of the body in the suckerless Polyclads (Acotylea) may be largely due to curious granular vesicles of unknown significance lying in the ectoderm (Lang, *Die Polycladen*, 1884).

In the sucker-bearing Polyclads (Cotylea) pigment is deposited either in vacuolised cells of the ectodermal epithelium or in non-vacuolised cells of the mesodermal parenchyme. In the former case the pigment is mostly yellow,

orange or red, and consists either of coloured fluid within the vacuole alone, or of granules found in the peripheral protoplasmic portion of the cell and subsequently dehisced into the fluid contents of the enlarging central vacuole. The mesodermal pigment is in the form of black or brown granules deposited in the peripheral portions of the cells. The two kinds of pigment—bright ectodermal and dark mesodermal—may exist separately or together, and the general colour of the Planarian depends upon the preponderance of one or other of the different elements.

4. *Nemertea.* The brilliant colours of these animals are said by M'Intosh and Hubrecht to be due to pigmented cells of the connective tissue. Bürger, however, has shown (*Zeit. f. wiss. Zool.*, l., 1890) that in the most primitive Nemertines, *e.g.*, *Carinella*, the pigment resides, not in elements of the connective tissue, but in the non-glandular elements of the ectoderm. In all higher forms the pigment is contained in branched pigment-cells of the ordinary type, which are situated either entirely beneath the basement membrane of the ectodermal epithelium, as in Metanemertines, or partly above and partly below this membrane, as in *Eupolia*. In the latter case the pigment-cells are associated with the enlarged gland-cells of the ectoderm—a fact which suggests their derivation from the same embryonic layer.

5. *Hirudinea.* The pigment is entirely mesodermal, and is extensively deposited in cells of the connective and vasifactive tissues. The pigment found in the spaces between the mallet-shaped cells of the epidermis has intruded from the connective tissues (Lankester and A. G. Bourne).

6. *Annelida.* The bright orange colour of the Archiannelid *Dinophilus tæniatus* is due to pigment contained in large branched connective tissue cells. Orange-coloured granules are also contained in the cells of the nephridia (Harmer, *Jour., M. B. A.*, i., 1889).

According to Claparède (*Annélides Chétopodes du Golfe de Naples*, p. 158) the colours of Polychæte Annelids are generally due to pigment distributed in the chitinogenous, that is ectodermal, layer. The pigmented ectodermal cells

of *Hermione hystrix* differ, according to Jourdan (*Arch. Zool. Exp.*, v., p. 94, 1887), from the polygonal unpigmented cells of the same layer by their smaller size. Where the epithelium is columnar, as in *Telepsavus*, the pigment is contained in the outer portions of the cells (Claparède, *Ann. Sed.*, pl. xiii., figs. 9 and 19, 1873).

Pigment may also, however, be extensively deposited in the cells of the peritoneum, as in *Nereis peritonealis* and *perivisceralis* (Claparède). In the former case it is violet, in the latter brown in colour. "Chloragogen" cells—enlarged pigmentiferous cells of the splanchnopleure—are also widely distributed among Annelids. The blood in many Annelids also contains special highly coloured respiratory pigments.

Much-branched pigment-cells of a yellow or reddish-brown colour are found in certain otherwise transparent pelagic Polychætes, such as *Pontodora pelagica*, *Phalacrophorus pictus* (Greeff, *Zeit. f. w. Zool.*, xxxii., p. 237, 1879), and *Iopsilus phalacroides* (Viguier, *Arch. Zool. Exp.* (2), iv., 1886). They appear to lie in the connective tissue, and seem to have a certain relation with the nervous system. In form and arrangement they foreshadow the chromatophores of Crustacea.

In Oligochæta the pigments are generally mesodermal. Interesting exceptions to this rule are furnished by various species of *Æolosoma* and *Ctenodrilus*, in which a number of ectodermal cells scattered over the body are known to contain large oily drops, generally coloured in various brilliant tints of green (Von Kennel, *Arb. Zool. Inst. Wurzburg*, v., 1882 ; Beddard, *Proc. Zool. Soc.*, 1888).

7. *Gephyrea.* Respiratory and excretory pigments are common. The dermal layer of the skin of *Sipunculus nudus* contains numerous pigment aggregations, apparently cellular, the precise nature of which cannot be said to have been satisfactorily ascertained (Andreæ, *Zeit. f. w. Zool.*, xxxvi., 1882). It is interesting to note that in the larva somewhat similar bodies are found within the ectoderm. These are stated to disappear during the metamorphosis of the larva (Hatschek, *Wien Arbeiten*, v., 1884); but the

question arises as to whether they may not have some connection with the dermal deposits of the adult. Balls of pigmented cells also occur in the sub-epidermal tissues of Echiurids (Spengel, *Zeit. f. w. Zool.*, xxxiv., 1880).

8. *Crustacea.* Pigments may be deposited either in the ectodermal epithelium or in special highly branched sub-epithelial cells, usually referred to the connective tissue and known as chromatophores. The latter are chiefly found in Malacostraca, but are also known to occur among Ostracoda in various species of *Loxoconcha* (G. W. Müller, 1884). Crustacean chromatophores are usually highly mobile, and in Isopods, at any rate, the chromatophore is contractile as a whole (Matzdorff, *Jena Zeit.*, 1883). The presence of chromatophores is usually associated with transparency of the body, *e.g.*, Amphipoda, Schizopoda, Prawns; epithelial pigmentation naturally entails opacity, as in the larger Macrura and most Brachyura.

9. *Tracheata.* In *Peripatus* the characteristic colours of the body are due to pigment granules deposited in the protoplasm of the outer ends of the ectodermal cells (Balfour, *Q. J. M. S.*, 1883).

The same is true of Insects in general (Poulton, *Proc. Roy. Soc.*, xxxviii., 1885; *Trans. Ent. Soc.*, pl. x., 1887); and probably also of Arachnids. But the branched pigment-cells in the central eyes of Scorpions (and *Limulus*) and in the compound eyes of Insects are believed by Lankester and Bourne to be intrusive connective tissue cells (*Q. J. M. S.*, xxiii., 1883).

10. *Mollusca.* The integument is brilliantly coloured in certain Amphineura, *e.g.*, *Dondersia banyulensis*, but the exact localisation of the pigment is not described (Pruvot, *Arch. Zool. Exp.* (2), ix., 1891).

In Gastropoda the pigment occurs either in the ectodermal epithelium, as in *Haliotis*, *Neritina*, Heteropoda, *Doris;* or in the sub-epithelial connective tissue (Boll, *Arch. f. mikr. Anat.*, v., *Suppl.*, p. 51, 1869). In the latter case the pigment may reside in true chromatophores, as in Pteropods and Cephalopods, or in great glandular cells lying in the connective tissue but communicating with

the exterior by a narrow neck, and belonging really to the ectodermal layer (Leydig, *Arch. f. Naturg.*, xlii., 1876; Boll, *l. c.*). This type of pigmentation occurs in Pulmonata; but there is also in this group, just beneath the epithelium, a dense pigmented network, which consists, according to Leydig, of branched mobile pigment-cells.

11. *Echinoderma.* In Holothurians intracellular pigment may be restricted to a granular deposit in the ectodermal epithelium, *e.g.*, in *Stichopus regalis*, or may occur in the form of bead-like deposits along thread-like prolongations of the basal ends of ectodermal cells (Jourdain, *Ann. Mus. Hist. Nat.*, Marseille, i., 1883), or in the terminal fibres of the cutaneous nerve-plexus. Ludwig also mentions the existence of richly branched pigment-cells (*Bronn's Thier-Reichs*).

In Asterids the brilliant red and violet pigments are in the form of granules deposited in the cells of the external epithelium (Cuénot, *Arch. Zool. Exp.* (2), v., *bis* 1887-1890). The epidermal pigment-cells of the optic pits are prolonged at their bases into long threads enclosing bead-like deposits of pigment as in Holothurians (Hamann, *Beiträge*, Asteriden, Jena, pp. 17-19, 1885).

In Echinids the pigment is contained in branched contractile cells, which lie either in the connective tissue layer, in the space between the epidermis and the muscle layer, or in the epidermis itself. Hamann interprets these cells as wandering cells of mesodermal origin (*Beiträge*, Echiniden, pp. 22, 30, 43, 45, 53, 85, 1887).

12. *Tunicata.* Pigment is almost entirely restricted to the blood-corpuscles and other mesodermal elements, which are often vividly and variously coloured, *e.g.*, in *Botryllus*. Mesodermal pigmented cells may penetrate into the cellulose test. Ramified pigment-cells have been observed in *Salpa bicaudata* (Gegenbaur, Kölliker u. Müller, *Zeit. f. w. Zool.*, p. 331, 1853).

13. *Vertebrata.* The branched mobile chromatophores of Vertebrates occur both in the epidermis and the dermis, most frequently in the latter. Their structure is identical in the two cases, and on account of their greater frequency

in the mesodermal tissues and their resemblance in form to various unpigmented cells of the connective tissues the chromatophores both of the epidermal and subjacent layers are usually regarded as being of mesodermal origin.

Pigment is also frequently deposited in the ordinary unbranched cells of the deeper layers of the epidermis (Kölliker, *Handbuch der Gewebelehre*, Leipzig, 1889).

From the above survey it may be seen that although pigment-cells are widely distributed, they attain a high elaboration of form and function in relatively few phyla of the animal kingdom. In its highest form the pigment-cell is mobile and under the influence of the nervous system; but such chromatophores are found only among Vertebrata, among Cephalopod and Pteropod Mollusca, among Crustacea, and possibly in a few pelagic Annelida and Ctenophora. Branched pigment-cells are also found in Porifera, Nemertea, in the compound eyes of various Tracheata, in Pulmonate Mollusca, and in Echinoderms; but in these cases the pigment-cell is apparently incapable of those movements which in the chromatophore of the Cephalopod or Vertebrate cause marked alterations in the colour of the animal. It is even questionable whether the branched form of these pigment-cells is in any way connected with purposes of colour display. It is impossible to maintain that colour in itself is of any value to a sponge; and the pigment-cells of Echinids have clearly not been specialised for chromatic purposes, since the majority of them are situated within the shell where they cannot affect the coloration of the animal. Moreover, in Holothurians pigment-laden wandering cells have been shown to discharge an excretory function (Schultz, *Biol. Centr.*, xv., p. 390, 1895). The function of the pigment-cells in Nemertea and Pulmonata is quite problematic; but a nutritive or excretory function could be assigned to them with just as much, or little, reason as could a chromatic function.

If we now take into consideration the immobile unbranched type of pigment-cell as found among the Turbellaria or the Oligochæta *Æolosoma* and *Ctenodrilus*, we again find that the modifications which these cells exhibit

are not clearly correlated with any chromatic function. The entoplastic modifications shown by these pigment-cells are in no way different from those which characterise ordinary storage cells of reserve or waste materials.

It would thus appear that the only pigment-cells distinctly specialised for chromatic purposes are those of Vertebrata, of Cephalopod and certain Pteropod Mollusca, and of Crustacea. To these pigment-cells the term chromatophore should be at present restricted, though it is very probable that the mobile pigment-cells of certain Ctenophores and the branched pigment-cells of certain pelagic Annelids will eventually find a place in the same category.

We are now in a position to confront the question of the origin of chromatophores. Have these remarkable elements arisen independently of the remaining types of pigmented cells, or have they been formed from pre-existing pigmented cells specialised for chromatic purposes? Also, do chromatophores exhibit any constant relation to the germinal layers?

The answer to these questions can only be given after a separate examination of the history of the chromatophores in each group. Before proceeding to this examination it may be well to point out the following considerations which are not without weight as guides to the formation of an opinion upon the subject.

The usefulness of pigment for chromatic purposes could only begin after the pigment had originated, and it is therefore probable that chromatophores have arisen by the modification of pre-existing pigmented cells. Moreover, since the prime necessity of chromatophores is that they should be visible, it is probable that they would arise in the external layer of the body, the ectoderm. This view is at variance with current opinion, according to which chromatophores are of the nature of connective tissue elements; but I shall show that there are many facts in the history of chromatophores which are quite irreconcilable with this opinion, and that the body of evidence strongly supports the view which I am propounding.

In the first place the branched contractile cells of

Ctenophores are indubitably ectodermal both in origin and position; and I shall show below that the chromatophores of Cephalopods which are mesodermal in position are ectodermal in origin.

In the second place it can be shown that pigment-cells which are usually sub-epidermal in position in certain groups have in all probability migrated inwards from the ectoderm. The Nemertea offer good examples of this phenomenon. In the Protonemertini, *e.g.*, in *Carinella*, which possess no cutis, the pigmented cells form part of the ectodermal epithelium (Bürger, *l. c.*, taf. ix., fig. 123); and the Metanemertini, or Enopla, retain this primitive condition (*l. c.*, p. 178, fig. 127). But the Heteronemertini possess a subepithelial layer or cutis which is not found in the other groups, and branched pigment-cells are contained within this layer. Deeply as the pigment-cells extend in many forms, *e.g.*, *Lineus gesserensis*, they are confined to the external glandular layer of the cutis in the most primitive Heteronemertines, *e.g.*, *Eupolia*, and in *Eupolia Brockii* the pigment-cells are only partially contained within the cutis, their upper extremities stretching between the epithelial cells to the external surface of the epithelium (Bürger, *l. c.*, pp. 33, 50, fig. 26). The series is complete, and there can be scarcely a doubt that the pigment-cells of Heteronemertines are ectodermal elements which have sunk beneath the epithelium *pari passu* with the elongation of the ectodermal glands.

In certain Gephyrea pigment-cells are found within the cutis of the adult; and in the case of *Sipunculus nudus*, at any rate, they are known to be preceded by pigmented bodies in the ectoderm.

Among Crustacea Malacostraca the chromatophores are situated in the mesoderm in the higher forms. But they have been observed in the ectoderm in some Isopods, and just beneath it in others; in the latter case they often possess processes which stretch up through the epithelium to the cuticle above it.

Again, in Echinoderma we have seen that in certain cases the pigment is contained in prolongations of the

ectodermal cells beneath the general layer of the epithelium.

Finally, Kerbert's (33) interesting observations on Vertebrata have shown that during the development of reptiles the chromatophores appear first in the epidermis, and only subsequently in the cutis. In the Lacertinæ a certain number of chromatophores are retained in the epidermis even in the adult; but in snakes, whose scales attain a higher degree of differentiation than is the case with those of lizards, no chromatophores are retained in the epidermis after embryonic life; the epidermic stage of the chromatophores in snakes is transitory.

It would thus appear that there is a considerable amount of evidence in favour of the view that chromatophores in general are of ectodermal origin, whatever be their ultimate position in the body.

THE CHROMATOPHORES OF CRUSTACEA. The literature which bears upon the subject of chromatophores in Crustacea deals chiefly with the sessile-eyed Malacostraca, and the investigations which point to the ectodermal origin of chromatophores deal principally with certain Isopoda.

In *Trichoniscus*, according to Max Weber (1), the ectoderm is a syncytium and consists of nuclei embedded in a granular sheet of protoplasm beneath the chitinous cuticle. Only here and there, for example at the junction of two segments, can a definite epithelium be distinguished. The chromatophores lie partly in the connective tissue of the body cavity, and partly in a layer just beneath the ectoderm. In the latter case, however, although the bodies of the chromatophores may lie beneath the ectoderm, many of their processes are found within the syncytium itself and often extend as far as the under surface of the cuticle. Here and there indeed entire chromatophores are found embedded in the subcuticular syncytium, and their branches, anastomosing with those of neighbouring chromatophores, form a net-work within the syncytium, which often produces the appearance of a regular epithelium, especially when the meshes of the net-work happen each to enclose one of the nuclei of the syncytium. In *Trichoniscus*

Leydigii, which is a true cave animal, branched cells are present in the subcuticular syncytium, which resemble the chromatophores of allied types in all points except that pigment is not deposited within them.

In *Idotea*, according to Matzdorff (2), the chromatophores lie exclusively in the epidermis. This consists of two layers in *Idotea*, an outer epithelium of chitinogenous cells and an inner granular syncytium with regular distributed nuclei but without cell-boundaries. The chromatophores lie in this under layer, and occupy its whole thickness, even bulging slightly into the epithelial layer above and into the connective tissue below. Each chromatophore is a naked nucleated cell without a bounding membrane. Its shape can vary from a spherical or oval to a highly stellate form. The processes bore their way through the protoplasm of the syncytial layer without having any definite paths prescribed for them; and the branches of neighbouring chromatophores can fuse to form an intricate net-work of pigmented tissue. The chromatophores of Isopods are true amœboid cells whose resting condition is that of contraction, and whose active condition is that of expansion.

In Caprellids, according to Paul Mayer (3), the epidermis is cellular, and forms a true pavement epithelium which is one-layered throughout—a statement which he would extend to Arthropoda in general. He agrees with Hoek (4) that the chromatophores are exclusively situated in the connective tissue, and in the envelopes arising from it which surround the gut, nervous system, gonads, and heart.

We thus see that, if the observations of Max Weber and Matzdorff be well founded, the Crustacean chromatophore, though frequently assuming a mesodermal position, is very probably of ectodermal origin. Mayer's generalisation that the epidermis of Arthropods is universally one-layered cannot be absolutely accepted, for it has been shown by Viaillanes (5), Minchin (6), and Mingazzini (7) that in insects at any rate certain branched cells of the epidermis may be found beneath the general level of the epithelium.

I would place the chromatophores of Crustacea in the same category as these branched cells of the Insectan epidermis, and would draw attention to the fact, established by Max Weber, that in cavernicolous forms the chromatophores of the ectoderm are unpigmented, in which condition they closely resemble the branched ectodermal cells of insects.

THE CHROMATOPHORES OF MOLLUSCA. So much attention has been directed to the study of the pigment-cell in Cephalopoda that it is desirable to recall the evidence which exists as to the occurrence of chromatic cells in other groups of the Mollusca.

In *Phyllirhoë* remarkable cells containing a brilliant golden-yellow substance were described in 1854 by H. Müller and Gegenbaur (8). They are grouped in a pair of longitudinal bands, one along the dorsal, and the other along the ventral edge of the body. They are sub-epithelial in position, and their nucleus is easily recognisable in young individuals. They were found to exhibit two modifications of form; one of these so closely resembles that of the chromatophores of Cephalopods that, although no phenomena of contraction or expansion were observed in them, they were interpreted by Müller and Gegenbaur as of the nature of chromatophores. These curious bodies would well repay a renewed examination. According to Panceri (9) they have nothing to do with the phosphorescence exhibited by *Phyllirhoë*.

In Pteropods chromatophores were first observed by Kölliker, Müller, and Gegenbaur (10), and were fully described and figured by the latter naturalist in 1855 (11). Two kinds of chromatophores were recognised. The first type consists of a central pigment-cell surrounded by a close-set series of radial muscle-fibres, each of which possesses a nucleus and has thus the value of a cell. The whole structure is contained within a well-defined space bounded by parenchymatous connective tissue, which forms a wall for the attachment of the radial fibres. The central pigment-cell is expanded by the contraction of the radial fibres as in Cephalopods. This type of chromatophore was found in the fins of several species of *Tiedemannia* and of *Cym-*

bulia quadripunctata. The second type of chromatophore was found in *Tiedemannia chrysotincta*, and consists of a single stellate cell with much branched processes, swollen at their ends. The cell consists of an outer non-contractile membrane and a central hyaline fluid substance containing pigment granules in suspension. The hyaline substance is markedly contractile, and may concentrate itself with the pigment entirely within the central body of the cell, or may expand to the tips of the processes, leaving the central part of the cell empty. The processes frequently contain pigment in one half while the other half is empty.

It is clear that the first of these two types of chromatophore is allied to that found in the Cephalopoda, while the second closely resembles the chromatophore of Vertebrata, as described by Brücke in the Chamæleon, Lister in the Frog, and Ballowitz in the Fish.

With regard to the chromatophores of Cephalopods a mass of controversial literature has accumulated during the last twenty years, and has almost taken the form of another Franco-German war, owing to the way in which the principal investigators have grouped themselves around the central question. Harless's (12) early interpretation of the chromatophore as consisting of a central passive pigment-cell with radial contractile fibre-cells was confirmed by H. Müller, Boll (*l. c.*), and other writers, and has been generally accepted as correct. But Harting (13) in 1874 opposed this interpretation, denied the contractile power of the radial fibres, and concluded that the power of altering the form of the chromatophore must reside within the protoplasm of the central cell itself. He regarded the phase of contraction as the active phase of the chromatophore.

Harting's views have obtained no acceptance except in France, where with slight modifications they have been restated with considerable emphasis, though it cannot be said with satisfactory evidence, by Blanchard (14), Girod (15), and Joubin (16).

On the other hand, the investigations of Kliemensiewicz (17) have furnished a very convincing series of observations

in support of the generally accepted view. It is difficult, in the short space at my disposal, to do justice to this author's valuable memoir, but the following observations made by him may be quoted. The radial fibres are thin and band-like during the contracted condition of the chromatophore, but broader during the expanded condition. In embryonic chromatophores the number of radial fibres is less than in fully developed chromatophores; and, in correlation with this, the chromatophore in expansion exhibits fewer processes or angles in the embryonic condition than when fully developed. Each process of the pigmented cell corresponds to a radial fibre, and has every appearance of having been caused by the pulling out of the membrane of the central cell by the radial fibre at that point. This fact, together with that of the shortening and widening of the radial fibres during the expansion of the chromatophore, renders inevitable the conclusion that the expansion of the chromatophore is determined by the contraction of the radial fibres. Moreover, in spite of Harting's statement to the contrary, there can be no doubt about the fact that the process of expansion of the chromatophore is much more rapid than the process of contraction.

I may add that from observations made at Plymouth during the present summer, I have been able to satisfy myself of the correctness of all these observations, and at the same time to make others which have convinced me that the radial fibres are the active agents in the expansion of the chromatophore. If a piece of the mantle of a young *Loligo media* be placed in a weak solution of methylene blue, the tissues are gradually impregnated with the dye, and the radial fibres are eventually paralysed in the contracted condition. But it frequently happens that the fibres of one side of a chromatophore take up the pigment and are paralysed before those of the opposite side, in which case it is possible to observe a curious phenomenon. One half of the chromatophore remains permanently expanded to its full extent, while the other half displays the usual phases of alternate expansion and contraction. If it be true, as Harting, Blanchard and their supporters maintain,

that the expansion of the central pigmented cell is due to some inherent amœboid power residing in the cell itself, such a phenomenon as this would be in the highest degree remarkable. For it would imply that one half of the cell was dead, or had at any rate lost its normal contractility, while the other half was perfectly healthy. It is more fully consistent with the phenomena to hold that the one half of the chromatophore remains expanded because the radial fibres which are attached to it are contracted and dead, as their deep impregnation with the methylene blue enables one to see, while the other half of the chromatophore is still capable of the ordinary changes of form because the unstained fibres attached to it are still alive and capable of relaxation as well as of contraction. I have even seen instances of chromatophores in which the entire protoplasm of the pigmented cell was dead, and in which the pigment granules were aggregated into irregular patches and streaks instead of being evenly distributed. In such cases it sometimes happened that one or two of the radial fibres, which had taken up relatively little of the stain, could be seen to contract from time to time, entailing a corresponding extension of the central cell in the region of their attachment. The agency of the radial fibres in the expansion of the chromatophore may accordingly be regarded as satisfactorily established.

The exact innervation of the chromatophore has not yet been conclusively demonstrated. Harting's suggestion than the radial fibres are nervous in nature has been seen to be groundless by every subsequent observer; but Kliemensiewicz, in spite of many preparations, was unable to find any nerve-fibrils supplying either the central pigment-cell or the radial muscle-cells. That some kind of innervation exists, however, is perfectly certain from the physiological experiments of Léon Fredericq (18), Kliemensiewicz, and Krukenberg (19). Fredericq showed that the motor centre for the chromatophores resides in the subœsophageal nerve-mass, a conclusion confirmed with an abundance of new detail by Kliemensiewicz in the following year. From the chromatophoric centre pass motor fibres

to the pedal ganglia and their nerves, and to the visceral ganglia and their nerves, while afferent fibres reach the centre from the optic ganglia. Krukenberg's experiments with various alkaloids and muscle poisons showed the probable existence of peripheral ganglia in the skin, as well as of a central organ in the brain. Joubin is the first and as yet the only investigator who has offered a description of the nerves themselves, his results being based on the employment of methylene blue. The chromatophoric nerves of the mantle arise from the stellate (pallial) ganglia, and each branch terminates in a chromatophore. The terminal nerve-fibre, according to Joubin, is slightly swollen at its extremity and abuts directly upon the edge of the pigment-cell between two of the radial fibre-cells. This is the only point in Joubin's description which is not very satisfactorily demonstrated, and it is to be hoped that a point of so much importance may soon be examined again.

The most interesting part of Joubin's paper, however, is his description of the development of the chromatophore in the embryo of *Argonauta*, in which form the development is apparently less abbreviated than in other types of Cephalopod. Joubin shows that the pigmented cell, though ultimately embedded in mesodermal tissue, is originally one of the constituent cells of the embryonic ectodermal epithelium. At an early stage it becomes slightly larger than its neighbours, and then sinks beneath the surface of the epithelium at the apex of a pit-like invagination of the ectoderm. It then enlarges greatly, detaches itself from the epithelial pit, and becomes surrounded by mesodermal cells which transform themselves into the radial muscle-cells. The ectodermal invagination closes up.

In the Cephalopod, therefore, as in the Ctenophore, the pigment-cells are ectodermal; but in the Cephalopod, as in the Crustacean or the Nemertine, the pigment-cells separate themselves from the layer in which they have originated, and take up a secondary position within the mesodermal tissues.

In existing Cephalopods the pigment-cell is a true chromatophore, whose only demonstrable function is that

of contributing to the coloration of the animal. In its final stage it is rendered so complex by the number of accessory nervous and muscular structures which become connected with it, that the question may well be asked by what phylogenetic steps so elaborate an organ has been evolved. As an answer to this question I would invite comparison between the developing chromatophore of *Argonauta* as described by Joubin, and the unicellular "purple-glands" of the mantle-edge of *Aplysia* as described by Blochmann (20). In *Aplysia limacina* each of the purple gland-cells is at first a part of the ectodermal epithelium; it enlarges and sinks beneath the epithelium, retaining only a narrow, neck-like prolongation to the surface; the whole of the cell then sinks deeper within the mesoderm, but its connection with the exterior is retained by the simultaneous development of a multicellular duct of ectoderm cells formed by invagination of the epithelium. Each gland-cell also becomes surrounded by connective tissue cells and muscle-cells, by the contraction of which the pigmented secretion of the gland is forced to the exterior. The striking histological resemblances between these unicellular glands of *Aplysia* and the chromatophores of Cephalopods did not escape Blochmann's notice; but now that Joubin has furnished us with embryological proof of the ectodermal origin of the chromatophore, and has figured an ectodermal invagination which corresponds in all respects to the multicellular duct of the gland-cell in *Aplysia*, it becomes possible to suggest distinct homologies between the two sets of structures. The developmental stages of the chromatophore in *Argonauta* appear to me to be largely recapitulative of its past history; and I would suggest that the chromatophores of Cephalopods have been evolved by the progressive modification of some such complex ectodermal gland as that of the mantle-edge of *Aplysia*. The only serious difference between the two structures is that in the Cephalopod the peripheral muscle-cells expand the pigment-cell, whereas in *Aplysia* they contract it. Kliemensiewicz, however, maintains that in addition to the radial muscle-fibres there is a distinct cellular envelope

around the pigment-cell which is the active agent in the contraction of the chromatophore. These cells, which correspond to the basilar cells of Girod (15), may be the homologues of the peripheral cells in *Aplysia*, while the radially elongated cells may be of more recent origin.

Whatever may be thought of this suggestion, it certainly seems to me significant that complex chromatophores of the Cephalopod type are also met with in certain Gymnosomatous Pteropods, as has been described above,—a group of animals which Pelseneer has conclusively shown to be closely related to the Aplysioid Opisthobranchs.

THE CHROMATOPHORES OF VERTEBRATA. The chromatophores of fishes have recently been studied from the physiological point of view by Cunningham and MacMunn (21), and from the histological by Ballowitz (22, 23). It is of course with the morphology of chromatophores that we are especially concerned in the present article; but some of the observations made by Cunningham and MacMunn bear upon one of the points which have been raised. In the pipe-fish *Siphonostoma*, the chromatophores are stated to lie so deep as to form a black sheet over the dorsal surface of the peritoneum; while in the flounder, *Pleuronectes flesus*, and to a less extent in the dab, *P. limanda*, pigment exists in the form of irregular branched masses between the epidermal cells, often resembling the dermal chromatophores in form, "as though some of the latter had bodily migrated into the ectoderm".

In the eel Waymouth Reid (24) has recognised the cellular nature of the branched pigment masses in the ectoderm, and is strongly disposed to regard them as intrusive mesodermal cells. This is the view which Kölliker (25) was the first to propound as a result of his observations on *Lepidosiren*. In this form numerous pigmented ramifications are found in the epidermis, but the bodies of the cells from which they arise are situated in the superficial layer of the cutis. In the sturgeon, H. Müller found entire pigment-cells within the epidermis, and regarded them as branched ectodermal cells; but Kölliker suggested that they had intruded from the cutis, *Lepidosiren* presenting a

condition of things which may be interpreted as an early stage in the process of migration.

It is impossible to come to a decision upon this important matter, for embryological observations upon the point seem to be entirely wanting.

Ballowitz's investigations deal partly with the phenomena of movement exhibited by the chromatophores of fishes (22), and partly with the details of their innervation (23). He confirms Solger (26) in his observations that during the contraction of a chromatophore only the inner pigmented protoplasm of the processes is withdrawn, while the outer protoplasmic envelope persists *in situ* in the form of a delicate unpigmented strand radiating out from the central pigmented mass. By the use of Golgi's method these unpigmented envelopes of the radiating processes may be stained in all their ramifications, and can thus be shown to remain permanently fixed, even during the maximum concentration of the pigment within the cell.

Reference may here be made to Guitel's memoir upon *Lepadogaster* (27), in which this investigator has also described the predetermined paths which the pigment takes during expansion of the chromatophore. On Plate xxviii. he figures a chromatophore in different stages of expansion.

Ballowitz further describes for the first time the remarkable nature of the innervation of the chromatophores. The motor nerve-fibres arise from the nerve-plexus in the skin, or frequently from the cutaneous nerves themselves prior to the formation of a plexus. The same motor nerve often supplies many adjacent chromatophores, and the chromatophores are supplied with a very variable number of motor branches, often one, but usually several or many. Peripheral ganglion cells are absent. Near the periphery of the chromatophore the motor fibre usually divides. One branch generally goes more or less directly towards the centre of the chromatophore, the other takes a more peripheral and spiral course over its surface. Both branches divide dichotomously into numerous twigs which terminate in "end-swellings" in the fixed unpigmented envelope of the chromatophore. Moreover, here and there a fibre pene-

trates the substance of the cell and reappears on its lower surface, winding and branching on this surface in a spiral manner in the same way as on the upper.

The chromatophore may thus be described as a disk lying between a pair of horizontal nerve-plates, consisting of spirally wound fibres and terminal swellings, the two plates being here and there in communication through the substance of the cell.

In Amphibia the development of the chromatophores appears to have been almost as little studied as in the case of fishes. The deep pigmentation of the ectoderm in embryos of the common frog supplies some ground, however, for believing that the chromatophores of Amphibia may ultimately be referred to the same embryonic layer, a view which has been defended by Jarisch (28), who maintains that the chromatophores in the epidermis are modified ectodermal cells. Ehrmann (31) states that the epithelial pigments of the Salamander are deposited by wandering cells.

The histology of Amphibian chromatophores has recently been studied by Biedermann (29), whose observations are in close agreement with those of Ballowitz upon fishes, and for the most part confirm the earlier statements of Sir Joseph Lister (30). Biedermann compares the movement phenomena of chromatophores with those of Rhizopods, which possess an external sluggish "hyaloplasm" and an internal more fluid "granular plasm". We may, however, refer to Lister's paper for evidence that the streaming movements of the pigment in Amphibian chromatophores are confined to the pigment granules; the fluid plasm in which they are suspended appears to be left behind in the branches of the chromatophore when concentration of the pigment sets in. Lister adds that the hypothesis which would seem most consistent with the phenomena of expansion is that of a mutual repulsion on the part of the pigment granules induced by some agency strongest at the centre of the cell and feeble in the remotest branches of the offsets. Reading this in the light of Ballowitz's recent demonstration of the situation of the chromatophore between two nerve-

plates, one is tempted to hazard the suggestion that the nervous discharge may actually pass through the chromatophore from one nerve-plate to the other, and after the manner of an electric discharge supply the agency necessary to induce mutual repulsion or attraction on the part of the pigment granules.

In reptiles, Brücke's paper on the Chamaeleon (32) remains classical. It was in this paper that Brücke showed for the first time that during the so-called "contraction" of the chromatophores in Vertebrata, the processes or branches are not themselves withdrawn, but merely the pigment within them.

I have already drawn attention to Kerbert's observations (33) on the development of the chromatophores in snake embryos; the branched pigmented cells appear in the epidermis before they are recognisable in the mesoderm. But Kerbert himself by no means holds that the chromatophores are therefore of ectodermal origin. At the stage when pigment first arises in the ectoderm he finds that both ectoderm and mesoderm contain a number of round or oval cells enclosing a central fluid vacuole; and he interprets these cells as the young stages of the chromatophores. He regards them as connective tissue cells which penetrate into the epidermis, develop pigment granules, and acquire a branched form. The only serious objection that can be urged against this view is that the author does not establish it. He shows us the vacuolated cells in both layers, and the branched pigmented cells in the epidermis; but he does not show us the vacuolated cells becoming chromatophores, although he makes the statement that here and there the vacuolated cells may be seen to be obviously filled with pigment. This is, however, not quite consistent with one of his earlier statements to the effect that pigment first appears in the ectoderm in the form of branched cells only slightly pigmented, the granules being confined to the edges of the cells, and occurring to a slight extent in the processes.

Kerbert finds it difficult to account for the appearance of chromatophores in the ectoderm, since in the adult snake

they are absent from that layer. He dismisses it as probably a "phenomenon of heredity".

The same investigator finds branched pigment-cells in the epidermis of an embryo chick of fifteen days. Here also he regards them as intrusive connective tissue cells, although a difference from those of Viper embryos is found in the fact that the pigment-cells already form pigment while still within the connective tissue. Remarkably enough, the pigment-cells both of the epidermis and of the cutis are stated to disappear completely by the twenty-third day.

In Mammals branched pigment-cells are frequent both in the epidermis and the cutis, but their origin is a subject of much dispute. An excellent summary of the facts may be found in Kölliker (35), who, although inclining to the view that pigment-cells are for the most part of mesodermal origin, does not go to such extremes as Aeby (36), Halpern (37), and others, who deny the pigment-forming power of the ectoderm altogether.

The writings of certain investigators, *e.g.*, Karg (38), Halpern (37), betray signs of a certain physiological preconception as to the function of pigment-cells, which it may be well to deal with here. Karg is especially emphatic upon the great *rôle* which intrusive pigment-cells must play in the nourishment of the epidermis, while Halpern assures us that the cells of the *rete Halpighii* take up pigment through the breaking down of pigment-laden wandering cells, and through absorption of parts of their protoplasm. It is clearly imagined here that the pigments in these cases are supplies of food material; but it may be asked whether the chromatophores of Fishes, Amphibians, and Reptiles are also stores of reserve material. They are well known to be nothing of the kind, and unless we deny the homology between the pigment-cells of Mammals and the chromatophores of the lower Vertebrata, we can afford to be sceptical about views as to the nutritive value of pigment-cells in Mammals. It seems to me to be much more probable that the pigment-cells of Mammals are simply degenerate representatives of the chromato-

phores of the lower Vertebrata. The ancestors of the Mammalia no doubt agreed with existing Amphibia and Reptiles in possessing chromatophores, but these would become useless as soon as the development of hair concealed the skin from view. The same argument may be employed in the case of birds, whose coating of feathers would also render chromatophores of no further use. Hence their degeneracy in birds and Mammals. That they are not necessary for the nutrition of the epidermis is well seen in the case of Primates. In Anthropoid Apes the epidermis contains not only processes from cutaneous pigment-cells, but frequently entire cells as well (Kölliker, 34). In the negro there are no entire pigment-cells in the epidermis, only processes from sub-epidermal cells (Karg, 38; Kölliker, 35). Lastly, in the white races of man pigment-cells are almost entirely absent, and are limited to certain special parts of the body (nipple, scrotum, etc.).

If I have thus rendered it probable that pigment-cells in Mammals have *not* the value of nutritive cells, perhaps this fact may reduce the bias which at present exists towards the view of their imagined mesodermal origin.

It is, of course, perfectly possible that the pigment-cells of Mammals are not homologous with the chromatophores of the lower Vertebrata, and have a nutritive function. That would be a very interesting point to decide.

Here my article must close. The literature upon pigment-cells is enormous, and the study which, for purposes of my own, I have made of it will not only, I trust, lighten the labours of some of my fellow-naturalists who are interested in the subject of animal coloration, but may possibly be serviceable in showing the paths along which new research can most profitably be conducted.

I have been astonished to discover that, so far as I am aware, there is not within the whole of existing literature a single indubitable proof of the mesodermal origin of true chromatic cells, and I have been unexpectedly led by my survey of the facts to the opinion that chromatophores, as defined at the beginning of this article, are universally of ectodermal origin.

How near to the truth, or how far from it, this generalisation is, it must remain with future researches to decide; but it should be borne in mind that the origin of the chromatic cell is by no means necessarily bound up with the origin of the pigment which it contains.

The subjoined classification indicates the relations of the different kinds of chromatophore which have been discussed above.

I. *Autoplastic.* Form-changes intrinsic.
   1. *Holoplastic.* Contractile as a whole, *e.g.*, Ctenophora, Isopoda.
   2. *Endoplastic.* Inner protoplasm alone contractile, *e.g.*, Vertebrata, certain Pteropoda.

II. *Alloplastic.* Form-changes extrinsic, *e.g.*, Cephalopoda, certain Pteropoda.

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WALTER GARSTANG.

THE SPACE RELATIONS OF ATOMS.

(*Continued.*)

THE attempt to advance beyond the distinction between two- and three-dimensional molecules, and to assign a definite form even to the least complex of atomic aggregates has been found full of difficulty. In its simplest form the problem is to find the relative position of the centres of gravity of the atoms in a state of rest, *i.e.*, at the absolute zero. The fact that in the case of a diatomic molecule these points must be in a line, and, in a triatomic molecule, in a plane, does not help us unless we can determine the relative lengths of the lines joining different atom-centres, which at present we cannot. Above the temperature of absolute zero complications are introduced by the motions of the atoms, and as to the extent and direction of these motions we know practically nothing. And in Van't Hoff's view all inferences drawn from the movements of an atom within a molecule are liable to an objection at the outset. The objection is that the moment an atom begins to move within a molecule it is liable to move out of the molecule altogether.

Van't Hoff argues—and the generalisation is as striking as it is simple—that it is only at absolute zero that a molecule is internally stable, seeing that all molecules must be supposed to undergo dissociation at a sufficiently high temperature, and experiment and theory agree in showing that though dissociation diminishes with the temperature, it would never cease short of the absolute zero. Above this temperature, then, the equilibrium of a molecule always depends on its exchanges with others.

The inference is that atomic motion should, for the present, be ignored in our attempts to determine atomic positions. Indeed the argument apparently points to atomic chaos as the only state possible above absolute zero ; but the inter-molecular exchanges may be supposed

to take place always at the same phase of the oscillation of an atom so as not to interfere with the periodic nature of the oscillations, and Van't Hoff admits that "he who prefers to assume atomic motion may consider the points, described as stationary, as positions about which the motion, probably periodical, takes place".

This has from the first been the attitude of Van't Hoff, though the doctrine of universal dissociation appears only in the latest edition of his book (1894); and it was natural that in its inception stereochemistry should take this trend, seeing that its first task was to account for cases of "abnormal" isomerism, and that it was only later it began to concern itself with "abnormal" reactions, and therefore with the problem of atomic dynamics.

It was the discovery by Wislicenus in 1869 of a second active lactic acid, which, following on the work of Pasteur already mentioned, forced chemists to see the insufficiency of the ordinary structural formulæ, of which there is only one for these two substances, *viz.*, $CH_3.CH.OH.COOH$.

At this time attempts at three-dimensional formulæ had already been made; various chemists had devised models for the purpose of illustrating the binding-power or valence of the various atoms, each binding-unit being represented by a rod attached to the sphere which stood for the atom; these rods were generally all in one plane, and Kekulé was the first (1867) who, in order to represent the power of a carbon atom to combine with another by one, two, or three of its units of valence, directed the rods in this case towards the corners of the tetrahedron described about the carbon-sphere. For a time the influence of Wislicenus' discovery on such speculations was not apparent; thus in 1873 there was published Gaudin's *L'architecture au monde des atomes dévoilant la structure des composés chimiques et leur crystallogénie*,[1] in which the author is guided entirely by certain laws of symmetry similar to those which apply in crystallography; and in 1875 F. W. Clarke[2] in a paper called "Chemistry in Three Dimensions" argued that the monatomic

[1] Paris, Gauthier Villers.

[2] *Proc. Am. Ass. Adv. Sci.*, p. 99, 1875.

atoms must always occupy the periphery of the molecule because of their readiness to react, and from the forms of crystals he concluded that all molecules must possess three dimensions. These speculations only served to illustrate the sterility of theories which cannot be submitted to definite practical tests.

Meanwhile, in 1873, Wislicenus had published in greater detail the proofs that the two active lactic acids possess the same structural formula, and had again urged, as he had done earlier, that the difference in their properties must be accounted for by a difference in the space relations of their atoms. At this point, and inspired by this doctrine, Van't Hoff took up the subject in 1874; a little later in the same year Le Bel's first paper appeared; and the results of Pasteur, of Kekulé, and of Wislicenus appeared as connected parts of one harmonious whole, when seen in the light of the theories thus almost simultaneously published, and now recognised as the basis of modern stereochemistry.

The basis of Van't Hoff's theory was a tetrahedral configuration for the groups attached to a carbon atom; this shows two configurations for the active lactic acids (fig. 5,

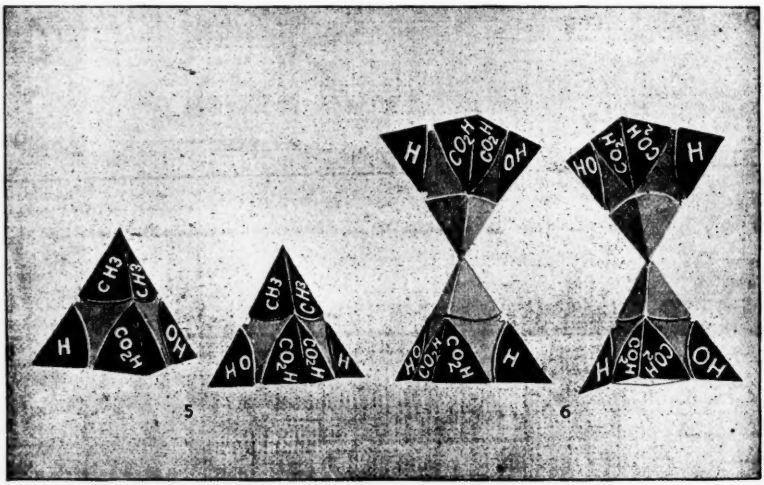


PLATE I.

Plate I.), and in general two configurations for $CR'R''R'''R^{iv}$ which become identical when two R-groups become iden-

tical, giving only one $C(R')_2R''R'''$; whereas a plane formula must have at least two configurations for this substance, representing two isomers:—

where only one actually exists. For a similar reason preference must be given to the tetrahedral grouping for $C(R')_2(R'')_2$; for $C(R')_3R''$ and for $C(R')_4$ both the solid and the plane formulæ accord with the facts in representing only one configuration; but for these, too, Van't Hoff prefers the former.

"My fundamental idea was the tetrahedral grouping, that is to say, some force—cause unknown—proceeding from the carbon atom and tending to drive the groups united to carbon as far away from one another as possible, that is, to bring them into the tetrahedral position. Although it did not follow that the tetrahedron must be regular, because the mutual action of the different groups may vary it somewhat, yet the tendency to form the regular tetrahedron remained, and in the case of identity among the groups, as in CH_4, the tendency was realised" (*Atome im Raume*, p. 68).

As to this, Le Bel holds that it depends entirely on the relation between the attraction of C for H on the one hand, and the repulsion between H and H on the other. He assumes[1] that atoms attract one another up to a certain point, but on closer approximation repel one another. We have then for CR_4 two positions of equilibrium of R_4 about C. A symmetrical (regular tetrahedral) arrangement will result if the repulsive zones of R occupy the whole surface of the zone C or a greater surface; but if less, a non-symmetrical arrangement will result. (They

[1] *Bull. Soc. Chim.* [3], iii., 788.

cannot occupy much less surface, because then another R would have room to attach itself to C.) The first arrangement has the symmetry of the cubic system, the second that of the rhombic system; and for CR_3R' we should have a rhombohedral arrangement. And in fact we find CI_4 to be tetrahedral, CBr_4 rhombic, and $CHBr_3$ rhombohedral. But in the present state of our knowledge of the relation between chemical constitution and crystalline form, little weight can be attached to such coincidences.[1]

That the carbon atom really possesses a repulsive force, Le Bel infers from the ratio of the specific heats of marsh gas, which shows that the atoms do not touch; and he points out that, for carbon at least, the hypothesis of the repulsive zone dispenses entirely with the necessity for a valence-hypothesis. His objection to the valence-hypothesis is that, as ordinarily held, it attributes to the carbon atom, not merely an attractive force, but a directive force acting at right angles to this, and causing the attracted groups to take the tetrahedral position.

It will be seen from this paper, written by Le Bel to show how his views differ from those of Van't Hoff, that this difference is not so great after all. Le Bel's "repulsive zone" is represented by Van't Hoff's "force proceeding from the carbon atom, and tending to bring the groups connected with it into positions as far removed from one another as possible, that is" (but here Le Bel would add the qualification "unless the ratio of the repulsive zones is unfavourable") "into the tetrahedral position".

And, to quote another passage of Van't Hoff: "Historically the difference lies in this, that Le Bel's starting-point was the researches of Pasteur, mine those of Kekulé. . . . My conception is a continuation of Kekulé's law of the quadrivalence of carbon, with the added hypothesis

[1] For an account of the work of Sollas, Muthmann, Tutton, and Penfield on the arrangement of atoms in crystals, the reader is referred to the article by H. A. Miers in "SCIENCE PROGRESS" (iii., 129).

that the four valences are directed towards the corners of a tetrahedron, with the carbon atom in the centre. . . ."[1]

"Practically our ideas, so far as they concern the asymmetric carbon, amount to the same thing; explanation of the two isomers by means of the tetrahedron and its image, disappearance of this isomerism when two groups become identical through the resulting symmetry and identity of the two tetrahedra" (*Atome im Raume*, p. 2, 1894). As to whether an asymmetric atom—to the exclusion of an asymmetric group—is necessary for optical activity, Van't Hoff from the first regarded this question as settled in the affirmative by the test of experiment; as to why an asymmetric group should not be equally effective he offers no theory. With regard to the question whether an asymmetric atom is sufficient to cause optical activity Van't Hoff will admit of no exceptions; the apparent exceptions are due in his view entirely to the difficulty of "doubling" the inactive mixture.

The right- and left-handed relation of the isomers $CR'R''R'''R^{iv}$ in their action on light and their crystalline form has already been discussed.

It is to be noted, further, that all the molecular dimensions being equal in the two isomers, we must expect a kind of isomerism distinguished by a near approach to identity. Accordingly we find that both isomers possess the same specific gravity, critical temperature, boiling-point, melting-point, latent heat of fusion and vaporisation; in short, all the physical properties depending on molecular dimensions and attractions are the same.

As regards chemical properties, we find equal stability, the same speed of formation, equilibrium when equal quantities of each are present together, and equal heat of formation. This quantitative proof raises to mathe-

[1] Kekulé had already suggested this arrangement of the carbon-valences, as we have seen; but the great advance made by Van't Hoff was that he showed the practical bearing of this hypothesis on optical isomerism, on geometrical isomerism, and on ring-formation, in every case bringing the hypothesis to the test of experiment.

matical certainty the evidence in favour of the enantiomorphic formulæ assigned to the two isomers.

Various models have been devised to illustrate the tetrahedral configurations, and it cannot be too strongly urged that models of some kind are essential to a clear understanding of the subject. Van't Hoff used cardboard tetrahedra, with corner-caps differently coloured to represent the different groups. By placing four caps of different colours, in different order on each of two tetrahedra, we obtain the two asymmetric configurations related as object and image, representing the two isomers $CR'R''R'''R^{iv}$. But if we make two of the corner-caps of the same colour on each tetrahedron the two configurations become identical, and each possesses now a plane of symmetry. The same thing may be represented by the Kekulé models as modified by v. Baeyer.

A simple and inexpensive form of model has been devised by P. Friedländer,[1] and consists of four short pieces of caoutchouc tubing, symmetrically diverging from a centre where they are joined together (according to Van't Hoff with sealing-wax).

I am indebted to Mr. H. A. D. Jowett for a description of similar models, which any one may readily make for himself by attaching short rubber tubes plugged with cork to four equidistant points on a small, hollow rubber ball by means of tacks (head inside the ball) and rubber cement. This arrangement is of advantage if one wishes to represent the carbon atom as having an appreciable size compared with the distance between the atoms. Moreover, these models are more easily made of the requisite symmetry than are Friedländer's.

Another method is to solder together at the ends two brass rods, each bent at the middle at an angle of 109°; coloured rods, or balls, or flags bearing formulæ may be attached to the ends of the brass rods by means of rubber connectors.

While for private study it is desirable to use models as small as can be conveniently handled, for lecture purposes

[1] *Ber. d. Chem. Ges.*, xxiii., 572.

we need them as large as can be conveniently handled, and we may then use tetrahedra having corner-caps marked with the formulæ of the particular radicals attached to the carbon atom. Models of this kind have been described[1] under the name of "solid formulæ," and some of the plates illustrating them are reproduced here to represent the configuration of certain molecules.

To illustrate the fact that unlike groups are at unequal distances from the central carbon atom, models with unequal sides or limbs would be required, but for ordinary purposes the symmetrical models suffice, and are in fact always used.

With the aid of the models we may now follow Van't Hoff in his development of the formulæ of molecules containing connected carbon atoms.

Assuming that the radicals attached to an asymmetric carbon atom have the tetrahedral configuration, we must represent a compound with two connected carbon atoms, $CR'R''R'''$ $CR^{iv}R^{v}R^{vi}$, by two tetrahedra, each carbon atom occupying at once the centre of one tetrahedron and the corner of the other. In the models the tetrahedra are, for convenience, shown simply corner to corner (see the solid formulæ for tartaric acid, figs. 6 and 7, Plates I. and II.). Any other configuration obtained by the rotation of either tetrahedron about the axis C – C would be equally in accord with the fundamental conception; but we shall not therefore encounter innumerable isomers, for there will be only one of these configurations realised at any given temperature, *viz.*, the one favoured by the mutual action of the groups $R'R''R'''$ and $R^{iv}R^{v}R^{vi}$ at that temperature ("favoured configuration"). As change of temperature affects different groups differently, it is evident that if the change be carried far enough another configuration may become the favoured one, and there is evidence that in some cases this happens.

We may for convenience assume the configuration favoured at ordinary temperatures to correspond to the formula,

[1] Eiloart: *Am. Chem. Journ.*, xiii., 559; also *A Guide to Stereochemistry*. London: Clarence Eiloart, 1893. These models are now made by Messrs. Baird & Tatlock, according to samples approved by the writer. Models of the Friedländer type are supplied by the same makers.

$$\begin{array}{c} R''' \\ R'CR'' \\ | \\ R^{iv}CR^{v} \\ R^{vi} \end{array}$$

in which R′ is over R^{iv}, R″ over R^{v} and R‴ over R^{vi}. This plane formula may be considered as a projection of the model in which the front groups R‴ and R^{vi} are turned upwards and downwards respectively. "These projections may be used for illustrating the possible isomers. That there will be four of these will be at once evident, since each asymmetric carbon atom involves a doubling. These differences are represented by changing the order of the groups R′R″R‴. But if, without changing the order, we simply move R′ to R″, R″ to R‴, R‴ to R^{iv}, we only bring about the above-mentioned rotation, and no isomerism results. But if R′ and R″ change places we get a new isomer, also by transposing R^{iv} and R^{v}; hence the following symbols represent the four isomers. It is plain that these are reduced to two directly the asymmetry of one of the carbon atoms ceases, through R^{v} and R^{iv} becoming identical."

No. 1.	No. 2.	No. 3.	No. 4.
R‴	R‴	R‴	R‴
R′CR″	R″CR′	R′CR″	R″CR′
$R^{iv}CR^{v}$	$R^{iv}CR^{v}$	$R^{v}CR^{iv}$	$R^{v}CR^{iv}$
R^{vi}	R^{vi}	R^{vi}	R^{vi}

(Van't Hoff, *l. c.*, p. 37).

With three carbon atoms another doubling results, and there should be eight isomers, of which the formulæ may readily be constructed. And in general, for *n* carbons there should be *2n* isomers.

As to the character of the isomers, the formulæ show that they must occur in pairs, thus No. 1 and No. 4, No. 2 and No. 3, in the above series are enantiomorphous and alike in chemical properties, and in all physical properties except those which depend on their enantiomorphism; but each of the two pairs will differ from the other in activity, melting-point, solubility, etc.

In confirmation of the theory may be cited borneol and

its derivatives, which contain two carbon atoms, and exist in four isomeric forms occurring in two pairs, thus :—

r- and *l*-borneol α rotation $[\alpha]_D$ = + and − 37°.

r- and *l*-borneol β rotation ,, = + and − 33°.

Compounds containing three asymmetric carbon atoms should present eight isomers belonging to four types, and there have been actually prepared three types corresponding to the formula $CO_2H(CHOH)_3CH_2OH$, *viz.*, arabonic acid, xylonic acid, and ribonic acid. The corresponding acids with four asymmetric carbon atoms, $CO_2H(CHOH)_4CH_2OH$, should exist in sixteen different forms belonging to eight types; of these, eight isomers belonging to five types are known.

When the formula containing the asymmetric carbon is symmetrical the number of isomers is reduced, as identity results between what may be called the right-left and the left-right combinations, so that with the left-left and the right-right compounds we have altogether only three isomers for two asymmetric carbons; it has already been seen that this is the number of isomers presented by the symmetrically constituted compounds, tartaric acid and hydrobenzoïn. A corresponding simplification results for more than two asymmetric carbons.

To determine which configuration to assign to each isomer is often difficult, and to decide which of the two enantiomorphic symbols belongs to the right-rotating and which to the left-rotating compound is impossible. But in the case of tartaric acid, *e.g.*, we recognise the symbol $\begin{matrix} CO_2H \\ HCOH \\ HCOH \\ CO_2H \end{matrix}$, as belonging, on account of its symmetry, to the "inactive indivisible" type. This enables us to assign to that type of tetrose, $COH(CHOH)_2CH_2OH$, which yields inactive tartaric acid on oxidation, the symmetrical formula $\begin{matrix} H_2COH \\ HCOH \\ HCOH \\ OCH \end{matrix}$; while the other type, yielding active tartaric acid,

must have the formula $\begin{matrix} H_2COH \\ HCOH \\ HOCH \\ OCH \end{matrix}$, from which only the non-symmetrical acid $\begin{matrix} HCO_2H \\ HCOH \\ HOCH \\ CO_2H \end{matrix}$ can be derived. (Each of these types of tetrose corresponds with two isomers, right and left.) Through the experimental work of Fischer and Kiliani it has even been found possible to assign its proper formula to each of the seven known glucoses, $CH_2OH(CHOH)^4COH$, the guiding-thread being always the contion between inactivity and symmetry of formula among the derivatives, and between activity and lack of symmetry.

The configuration of the unsaturated compounds $CR'R''$ $CR'''R^{iv}$ is represented by placing the tetrahedral models edge to edge (see the solid formulæ for fumaric and maleïc

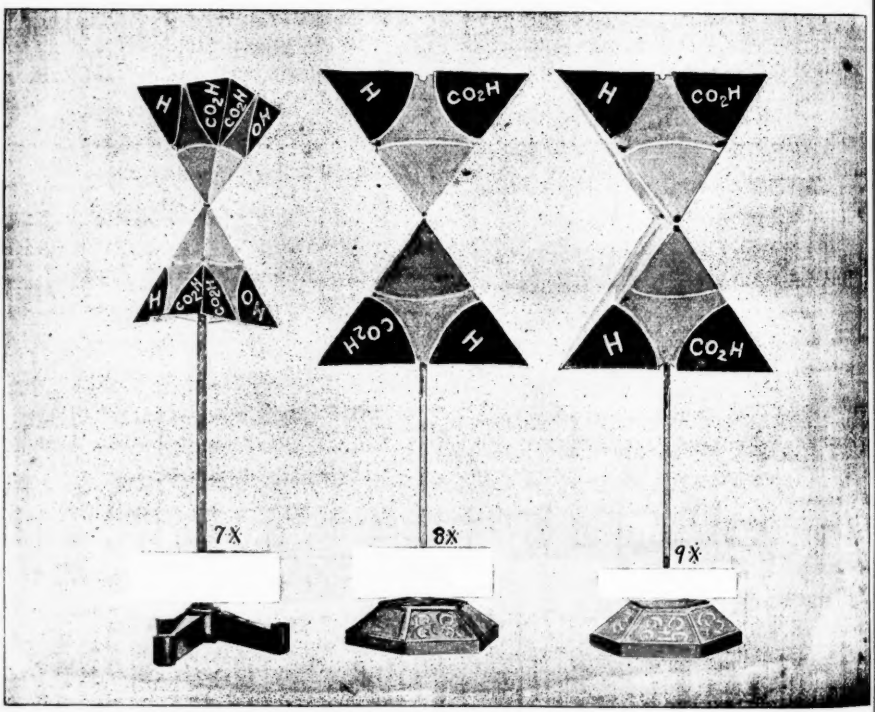


PLATE. II.

acids, figs. 7 and 8, Plate II.), although theoretically the tetrahedra should intersect to show the *rapprochement* of their centres. It will be observed that the R groups occupy one plane with the carbon atoms—a result foreseen by the tetrahedron-hypothesis (1874), long before it was proved (1882) by the reasoning already set forth. It is evident also that the tetrahedral configurations indicate the existence of the "cis-trans" isomers, which, without recourse to the models, may be indicated by the formulæ :—

$$\begin{matrix} R'CR'' \\ \| \\ R'''CR^{iv} \end{matrix} \qquad \text{and} \qquad \begin{matrix} R'CR'' \\ \| \\ R^{iv}CR''' \end{matrix}$$

The same isomerism will exist for CR′R″ CR′R″.

The character of this isomerism will be entirely different from that due to the presence of an asymmetric carbon. There is neither dissymmetry nor enantiomorphism in structure, and we shall expect therefore neither opposite optical activity nor hemihedry, and in fact we find none.

It has been made a reproach to stereochemistry that the same theory which explains the purely physical isomerism of the substances $CR'R''R'''R^{iv}$ is used to account for the pronounced chemical differences which characterise the isomers $C_2R'R''R'''R^{iv}$. But the new isomers lack the equality of molecular dimensions formerly observed; the theory is therefore perfectly consistent in demanding that they should differ in chemical as well as in physical properties. And Van't Hoff is now able to enumerate thirty-six cases of isomerism characterised by differences of this kind among bodies of the formula $C_2R'R''R'''R^{iv}$.

Van't Hoff was able at the outset to determine in certain cases which of the two formulæ belonged to each isomer, and since then Wislicenus has successfully attacked this problem in other cases. To this end these chemists considered in the first place the mechanism of the addition of atoms to a molecule, and in the second place the mutual influence of the indirectly connected groups.

In considering the addition of atoms to a molecule they relied on the principle of "least disturbance"; the structure of the molecule must be as little altered as possible. We

have already considered the addition of two hydroxyl groups to fumaric and maleïc acids respectively, and the proof that the acid (maleïc) which yields inactive tartaric acid $\begin{matrix}\text{OH}\\ \text{HC}\!\!-\!\!\text{COOH}\\ \text{HC}\!\!-\!\!\text{COOH}\\ \text{OH}\end{matrix}$ must possess the "cis" formula $\begin{matrix}\text{HC}\!\!-\!\!\text{COOH}\\ \text{HC}\!\!-\!\!\text{COOH}\end{matrix}$ depended on the assumption of the above principle, for it assumed that both the OH groups attach themselves to the same side of the molecule; or, in other words, that only one pair of tetrahedron-corners is separated to take up the two added groups; similarly the "trans" formula is proved for fumaric acid (compare the figures for fumaric, maleïc, and tartaric acid).

In considering the effect of adding atoms to two carbons trebly linked, we must remember that these are represented by two tetrahedra placed face to face, and that when one pair of corners is separated to take up two new atoms, two pairs of corners will remain joined, so that the added atoms will be on the same side of the molecule. On addition of bromine to acetylene-dicarboxylic acid we should get, then, $\begin{matrix}\text{CO}_2\text{HCBr}\\ \text{CO}_2\text{HCBr}\end{matrix}$, the "cis" or dibrom-maleïc acid. As a fact we get this acid, but at the same time there is formed twice as much of the other isomer $\begin{matrix}\text{CO}_2\text{HCBr}\\ \text{BrC}\!\!-\!\!\text{CO}_2\text{H}\end{matrix}$; the formation of the latter is, however, not surprising when we consider that it is much more stable than its isomer, which may be supposed to be the sole immediate product, and to undergo transformation while in the nascent state. The numerous similar objections to the theory which have been raised, especially by Michael, are similarly answered, for in every case the objection is the same, that instead of the expected product there is formed another which is more stable in the conditions of the experiment. Moreover, these objections refer exclusively to halogen-derivatives, which we have seen to be especially liable to transformation.

As when atoms are added to the molecule, so when they are abstracted from it, a difference between the isomers is

noted which may also be said to depend on the principle of least disturbance. The molecule $\begin{matrix} R'CR'' \\ R'CR'' \end{matrix}$ will suffer less disturbance in becoming $\begin{matrix} CR'' \\ CR'' \end{matrix}$ than will the molecule $\begin{matrix} R'CR'' \\ R''CR' \end{matrix}$; and accordingly it has been found by Wislicenus and his pupils that the rate of reduction in the same conditions is greater in the former case.

With regard to the mutual action of the R groups, we may say that the formula showing those groups which have the greater attraction for each other as occupying the same side of the molecule, will belong to the more stable isomer. Wislicenus assumed that the degree of attraction varied directly with the difference in positivity of the radicals R. But the matter appears to be not so simple. If, however, we have reason to assign to the less stable isomer the formula $\begin{matrix} R'CR' \\ R^{iv}CR''' \end{matrix}$, and to the more stable $\begin{matrix} R'CR'' \\ R'''CR^{iv} \end{matrix}$, we may test this by determining the heat of formation, which will always be greater for that isomer which is in an absolute sense the more stable; the proportion of this isomer formed at any given temperature may not be the greater, but as the temperature is lowered its proportion will increase until ultimately it preponderates.

Again when two groups in a compound readily react together, we attribute to them the "cis" position; hence, from its tendency to form the anhydride, maleïc acid must have this formula. The same conclusion may be drawn from its formation from ring-compounds; and that the negative groups are closer together in this compound than in its isomer is shown by the fact that its dissociation constant is twelve times higher.

The application of the tetrahedron-hypothesis to ring-compounds is illustrated by the figures of trimethylene derivatives, published by Van't Hoff twenty years ago; here the R groups occupy two planes, one on each side of that of the carbons; thus the arrangement for the trimethylene dicarboxylic acids which Buchner deduced, as we have seen, independently of the tetrahedron-hypothesis,

was long ago foreseen by it. The figures show also how "cis-trans" isomerism occurs in ring-compounds; when R′ changes places with R″ we get the other isomer.[1]

PLATE III.

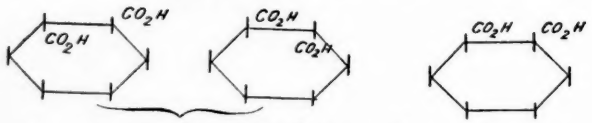
Among tetramethylene derivatives this kind of isomerism is encountered in the truxillic acids

$$C_6H_5CH - CHCO_2H \qquad C_6H_5CH - CHCO_2H$$
$$| \quad | \qquad \text{and} \qquad | \quad |$$
$$C_6H_5CH - CHCO_2H \qquad CO_2HCH - CHC_6H_5$$

of which at least four isomers are already known, and for which the theory foresees the existence of many more.

In every case where the R groups become identical, the isomerism vanishes; thus in the monosubstituted polymethylene derivatives it is non-existent. Again, the theory is borne out by the hexamethylene derivatives, hydroterephthalic and hydrophthalic acids, which may be shown in skeleton, thus:—

Hydroterephthalic acid.



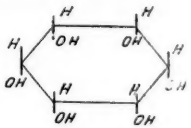
Hydrophthalic acid.

It will be seen that in the last case enantiomorphism exists, together with the "cis-trans" isomerisms, a complication

[1] Similarly in Plate III., hydrophthalic acid, if CO_2H and H be transposed.

observed in many other cases also. And in another hexamethylene derivative, inosite, which also possesses this kind of asymmetry, right- and left-handed isomers have been prepared.

The inosite formerly known being inactive and in divisible must have a symmetrical formula, thus :—



Other active isomers corresponding to other asymmetric formulæ have yet to be discovered.

Passing from hexamethylene derivatives to tetrahydrobenzol we still find stereo-isomers ("stereomers"), corresponding to the formulæ

Tetrahydroterephthalic acid.

And the isomerism continues so long as we have two R′R attached to the ring

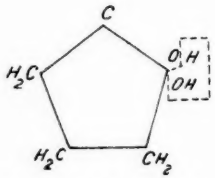
Dihydroterephthalic acid.

But just as the stereomerism of ethylene derivatives disappears when they are reduced to acetylene derivatives, so the stereomerism of the hydrobenzene derivatives disappears when they are reduced to benzene derivatives. And the reason is probably in both cases the same; the atoms are reduced to one plane; again the tetrahedral construction

is in accord with conclusions drawn independently of it from the observed inactivity of benzene derivatives.

The relative stability of ring-compounds, no less than the isomerism they present, has been attributed to the space relations of the carbon valences. If a chain of tetrahedron models be formed by joining them at one corner, it will be seen that, without bending the connecting rods, a free corner of the fifth may be made to all but touch a free corner of the first; so that to close the ring requires but a slight divergence of the linking valences from the angle of the regular tetrahedron, in fact the divergence is only 3°. In forming a hexa-, tetra-, tri- or di-methylene ring the divergence would be 11°, 19°, 49°, and 109° respectively; and it has been observed that the ease with which a ring is broken, corresponds to the divergence in question. Thus penta-, hexa-, and tetra-methylene rings are the most stable, whereas the trimethylene ring may be broken by means of bromine, and dimethylene is saturated even by iodine. Baeyer has applied the same theory to account for the explosive nature of acetylene and especially of polyacetylene compounds.

Returning to the chain of singly-linked carbons, we see that as the groups attached to the fifth carbon are nearer to the first carbon than are the groups attached to the fourth, so these are nearer than the groups of the third carbon. Accordingly we find that in an open chain of four carbons it is the groups attached to the end carbons, those which appear in an ordinary formula farthest apart, which are the readiest to react; *e.g.*, the γ- and δ-oxy-acids, which contain three and four carbon atoms between OH and COOH, are the readiest to form lactones in accordance with the formula



On making a chain of models with alternate double and single linkage, it will be found that the sixth carbon atom almost touches the first, thus indicating the superior stability of the benzene ring. ARNOLD EILOART.

THE SYNTHESIS OF PROTEIDS.

SINCE Wöhler, in 1828, succeeded in making urea artificially from its elements, the strides that organic chemistry has made have been prodigious. Complex substances previously made only in the living laboratory of plants and animals are now manufactured in the test tubes and retorts of the chemist. The substances which are of most importance to vital processes, the carbohydrates and the proteids, are among the last to yield before this advance. Fischer has, however, shown the way in which sugar may be made, but the synthesis of proteids, the most complex of all the compounds of carbon, is still not accomplished. There are, however, signs that this last conquest of organic chemistry cannot be far off, and when it has taken place we shall be nearer the settlement of many problems that now perplex the physiologist and the economist than we are at present. The vexed question of the constitution of albumin will be set at rest; light will be thrown upon many physiological processes that are at present obscure, and we shall be on the road to determine with accuracy the components of protoplasm, perhaps even in the distant future the manufacture of living material itself will not be such a hopeless task as it appears to be now. Economists who paint terrible pictures of how in a few centuries the land will be unable to support the increased population of the globe, will be comforted if only it is shown them that chemists will be able to make the substances which up to now we have relied upon nature to provide us with.

I propose in the following paper to briefly sketch one or two of the principal attempts that have been made in the manufacture of albuminous from simpler substances.

The products of decomposition of a proteid are extremely numerous, and vary with the method adopted for their decomposition. Briefly they fall into two groups, the fatty compounds generally containing an amidogen radicle, and the aromatic compounds or derivatives of benzene. Our

knowledge concerning these decompositions has been advanced by numerous chemists and physiologists, references to whose works will be found in a paper by Dr. Brodie in the September number of this journal. Among the names there mentioned it will be seen that Schützenberger's figures very largely, and to this observer belongs the credit of an attempt (one of the earliest conducted on scientific lines) to build up from the compounds he had obtained from albumin, something like the original proteid he had broken up (1).

In order to effect the synthesis of proteid material, he considered it necessary to combine a molecule of a leucine (*i.e.*, an amido-fatty acid) with a molecule of a leuceine (an amido-acid of the acrylic series) with elimination of water, and then to combine this complex group with one or more molecules of urea, and oxamide, also with elimination of water. The method he had adopted for the breaking up of proteids was boiling with alkalis ; this led to hydration, so in any attempt at synthesis he recognised as a *sine quâ non* the necessity of some method of dehydration.

The provisional formula he gives is the following :—

$H_2C_2O_4 + 2NH_3 + 3C_mH_{2m+1}NO_2 + 3C_nH_{2n-1}NO_2$ with elimination of eight molecules of water. This would give $C_{q+2}H_{2q-8}N_8O_8$, and if q = 28 the percentage composition calculated from the formula agrees closely with that of albumin.

Accordingly amido-compounds, leucines ($C_mH_{2m+1}NO_2$) and leuceines ($C_nH_{2n-1}NO_2$), were mixed with about 10 per cent. of urea and finely powdered. The mixture was dried at 110° C., and intimately mixed with 1·5 times its weight of phosphoric anhydride, and heated in an oil bath. At 120° there is no change, but at 125° dehydration takes place very rapidly, and the mixture becomes pasty, but solidifies to a compact product without any darkening. This was dissolved in water, the solution mixed with excess of alcohol, and the pasty precipitate so produced washed with alcohol and redissolved in water. Phosphoric acid was removed by means of baryta, and the filtered liquid when concentrated on a water bath, yielded an amorphous pro-

duct soluble in water, but was precipitated as a curdy mass on the addition of alcohol. Aqueous solutions of this product are precipitable by most of the other precipitants of proteids, namely, tannin, picric acid, mercuric chloride, Millon's reagent, potassium diiodide, mercuric potassium iodide, phosphotungstic acid in presence of hydrochloric acid, phosphomolybdic acid, and lead acetate and basic lead acetate. Potassium ferrocyanide, however, gives no precipitate in presence of acetic acid. With caustic potash and copper sulphate a rose-red coloration is formed. Heated with nitric acid the product becomes orange on adding ammonia, and when heated decomposes suddenly leaving a bulky mass of carbon. Its behaviour in this respect is similar to that of gelatin. When heated on platinum, the compound carbonises and swells up, giving the characteristic odour of burning nitrogenous animal matter.

We thus see that although Schützenberger succeeded in obtaining a substance very like albumin, yet the experiments are hardly conclusive because some of the characteristic properties of albumin are wanting, and the colour tests for proteid are given by many of the decomposition products of albuminous matter. His partial success will, however, point the way for future attempts, and so far as it goes is in favour of his theory of proteid constitution.

Some years previous to this, Grimaux (2) obtained by somewhat simpler processes substances which even more resembled proteids than Schützenberger's. He was especially interested in colloidal substances, inorganic and organic, but the three that he made which bear on the present question were the following :—

(A) Colloïde amidobenzoique. This is made by heating to 125° C. meta-amidobenzoic acid in sealed tubes with one and a half times its weight of phosphorus pentachloride for ninety minutes. The product, which is a white, friable powder, is washed repeatedly with boiling water to remove all phosphoric acid. The remaining substance is supposed by Grimaux to be an intramolecular anhydride formed by the union of several molecules of meta-amidobenzoic acid with the elimination of water. When ammonia is added it

dissolves slowly in the cold, but rapidly on heating. The solution obtained should be evaporated *in vacuo* at a low temperature. The resulting solid is a transparent jelly which dries into translucent, yellowish plates, which in their physical properties resemble dried serum-albumin.

(B) This colloid is similarly prepared, except that the temperature in the sealed tubes is allowed to rise to 135° C.

(C) Colloïde aspartique is prepared by the action of a current of gaseous ammonia heated to 170° C., on solid aspartic anhydride. The product is washed with water, and after evaporation *in vacuo* yields a substance similar in appearance to the colloid (A).

It will be seen from this that the obtaining of albumin by these methods was hardly to be expected, but rather one would get a product which would be, as it were, a skeleton of a proteid; in all cases heavy molecules were formed; in all cases the result was a colloid substance exhibiting, as we shall see directly, many of the properties hitherto deemed diagnostic of proteids, and in the case of the two first colloids there was present not only the amidogen, but also the aromatic radicle.

The resemblance between the proteids and these synthesised colloids is, however, remarkably close, and Dr. J. W. Pickering, who has been instrumental in bringing Grimaux's work prominently before English physiologists, has confirmed most of his results, and also discovered certain other similarities which were not noted by Grimaux. I take the following brief *resumé* of the chief of these similarities from Pickering's papers (3).

1. All give the xanthoproteic reaction.

2. With copper sulphate and caustic potash, A gives a blue violet; B, *nil;* C, a typical violet coloration.

3. Their solutions do not coagulate on heating in the absence of salt; if, however, a trace of a soluble barium, strontium, or calcium salt is present, opalescence occurs at 56° and coagulation at 75° C.

4. The colloids are removed from solution (rising to the surface of the fluid) by saturation with magnesium sulphate,

ammonium sulphate, or sodium chloride. Here they especially resemble the class of proteids called globulins.

5. Another resemblance to globulins is seen in their behaviour to a stream of carbonic anhydride, which in the presence of salts causes precipitation. The passage of a current of air through the mixture redissolves the precipitate.

6. The colloid B is not digested by pepsin-hydrochloric acid; A is slightly digestible; but C is easily digested, and then the solution gives the typical peptone colour, pink, on the addition of copper sulphate and caustic potash.

7. Each of the colloids when intravenously injected into animals (rabbits, cats, dogs, rats, guinea-pigs) causes extensive intravascular coagulation. In a typical experiment death is due to respiratory failure, and 5 to 20 c.c. of a 1·5 per cent. solution is usually fatal. The other symptoms noticed are pronounced exophthalmos and dilatation of the pupil; in dogs there is often hyperpnœa immediately before death.

This last property of the proteid-like colloids is the most remarkable of the series, and its discovery is entirely due to Dr. Pickering. The resemblance to the action of the nucleo-proteids is most marked, and extends even to minor points, *e.g.*, neither cause intravascular clotting in the blood of albino rabbits; and in dogs very minute doses indeed, cause a slowing of the rate of coagulation; but for these and other details the reader must consult the original papers.

I need hardly say that the result was an unexpected one, and it by no means lessens the difficulties surrounding the coagulation question. So far as was previously known only nucleo-proteids produced intravenous clotting, with the single exception of snake poison. Snake poison, however, produces extensive disintegration of the vascular wall, and so it was considered that this was the source of the nucleo-proteid. The artificial colloids produce on the other hand little or no disintegration of leucocytes, and no injury to the capillary walls, so that the same explanation will not hold here.

If nucleo-proteids and these colloids both produce the same effect in the same way, one is driven to the conclusion that their physiological activity is connected in the first place with the heaviness of their molecules, and in the second with the presence of some radicle common to both. The colloid condition will not entirely explain the action, since many colloids do not act in the same way; the active radicle is certainly not one which contains phosphorus, since all the colloids are free from that element; it may possibly be the amido-fatty radicle in a high state of condensation which is responsible for the clotting produced.

It is these two principal sets of researches that I wished to bring before the readers of "SCIENCE PROGRESS," because although both fall short of their ultimate object, the synthesis of proteid, yet they show the way to be followed in the future, and, moreover, they exhibit in themselves certain points of interest, of which the one treated last, the physiological action of Grimaux's colloids, is by no means the least.

I have not alluded in the foregoing paper to Lilienfeld's work on the synthesis of peptone. He has only brought the matter forward in a preliminary notice, and for important researches of this kind, one requires full details before their value can be estimated.

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W. D. HALLIBURTON.